THE DISEASES OF WARM COUNTRIES. A HAND-BOOK FOR MEDICAL MEN. SECOND REVISED EDITION

SCHEUBE

JEYES' MEDICAL PREPARATIONS.

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THE DISEASES OF WARM COUNTRIES

A Handbook for Medical Men

By Dr. B. SCHEUBE

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TRANSLATED FROM THE GERMAN

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WITH ADDENDA ON YELLOW FEVER BY JAMES CANTLIE, M.B., F.R.C.S. ; AND ON
MALARIA BY C. W. DANIELS, M.B., M.R.C.S.

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ANATOMY, CHARING CROSS HOSPITAL MEDICAL SCHOOL,
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many additional Plates, from "The Journal of Tropical Medicine"

SECOND REVISED EDITION

EDITOR'S PREFACE.

EVERY one who has read Professor Scheube's work in the original must have been struck by the accuracy of statement, the range of knowledge, the logical inferences, and the thoroughly scientific spirit which characterises the book. It must have occurred to all who read the book in German that its translation into English was most desirable, amounting indeed to a public duty, and the fact that Messrs. John Bale, Sons and Danielsson undertook the publication of a work of the kind, places those interested in scientific medicine and in Tropical Diseases deeply in their debt.

The work of editing the book has been rendered simple by the excellence and accuracy of the translation by Miss Pauline Falcke ; and if in some places the German idiom has been retained, it has been done advisedly ; for to attempt to transcribe it in every instance would but have served to detract from the virility of Professor Scheube's style.

Ever since Professor Scheube's work appeared in Germany, the desirability of reproducing the work in English has occurred to many. The magnitude of the task no doubt is the cause of the translation not being undertaken earlier, and the question of obtaining a sufficient sale for the work may have caused publishers to hesitate. It may be urged that some of the statements, in the light of research during the past twelve months, have lost their significance, but the general volume of information can never be refuted, but must remain for all time as a monument to Professor Scheube's labours, and as a comprehensive and accurate record of tropical diseases at the period of publication.

JAMES CANTLIE.

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   London, W., 1902.

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PLAGUE.

DEFINITION.

THE word *Plague* in ancient and mediæval times had a general pathological signification, every epidemic disease which swept off a large number of the people being, according to Galen, thus designated. In more modern times, however, the term plague has been limited to signify an infectious disease running a very acute course, attended by high fever, a serious general condition, and a high mortality. In the majority of outbreaks the bubonic type prevails,

SYNONYMS.

Λοιμός ; Pestis, Pestilentia, Febris pestilentialis, Pestis bubonica, Clades inguinaria, glandularia ; Beulenpest, Oriental Plague, Indian Plague, Black Death ; Plague ; Peste ; Pestilenza (Italy); Plaga (Spain); Peste bubonica (Portugal); Tschumá (Russia); Mahamari, *i.e.*, epidemic disease with great mortality, Gola, *i.e.*, Bubo, Phutkiya rog, *i.e.*, Bubo, Ghant ka rog, *i.e.*, Bubonic disease, Kokla ka rog, or Toa ka rog, *i.e.*, cough illness (India); Yang-tzu, *i.e.*, boil or itching wound, Yang-tzu-ping or Yang-tzu-chwang, *i.e.*, bubonic disease, Li-tzu, *i.e.*, bubo, Li-tzu cheng or Luan-tzu-chen, *i.e.*, egg illness, Schih-yi, *i.e.*, season-plague, Piarshe, *i.e.*, entangling viper, Shu-yi, *i.e.*, rat-plague, Wan-yik, *i.e.*, epidemic disease with great mortality (China); Malignant polyadenitis (Cantlie).

HISTORY AND GEOGRAPHICAL DISTRIBUTION.

The history of *Plague* may be traced back to a period dating from the end of the third or the beginning of the second century B.C. In Oribasius' Medical Excerpts there is a passage by Rufus of Ephesus, a contemporary of the Emperor Trajan (98-117 A.D.) in which plague buboes are described, and their appearance in epidemic form at this period in Libya, Egypt, and Syria mentioned. But the great epidemic which occurred during the sixth century was the first historically reliable account of the disease of which we are cognisant. This epidemic, which is usually designated the *Justinian plague*, because it occurred during the reign of the Emperor Justinian (527-565), spread over almost the whole of Europe, and lasted between fifty and sixty years. During the following centuries Europe was frequently visited by epidemics of plague. Yet none was more terrible, nor attained such dimensions as the pandemic of

the fourteenth century, known as the *Black Death*, "which as regards social and political conditions had the most terrible consequences ; it actually caused a loosening of all prevailing conditions, even of the most intimate family ties, and it had as a consequence, in the truest sense of the word, a deterioration of all social and friendly relations" (Pagel) No portion of the then known surface of the globe was spared by this visitation, and even distant Greenland was smitten and depopulated. According to Hecker's computation, twenty-five millions of persons, that is to say, a fourth part of the population of the Eastern hemisphere at this period, fell victims to this epidemic in Europe alone.

As the seventeenth century waned the epidemics in Europe occurred less frequently, and since the middle of the eighteenth century Western Europe until quite recently has been almost free from the disease. The south-east of Europe, Turkey, Caucasus, South Russia, Italy, Dalmatia, Greece, and the islands of the Mediterranean have, during the nineteenth century, been visited by epidemics from time to time. The last outbreak occurred in the year 1841. Since then Europe, with the exception of a small epidemic in the Government of Astrachan (Wetljanka), 1878-1879, has not been visited by plague until quite recent times, and it is only within the last few years that plague seriously threatened Europe.

The *European epidemics of plague* were all probably *imported from the East*, a fact that can be positively proved to be the case during the last century or two. The channel by which plague entered Europe hitherto has always been by way of Turkey, and it has invariably been Turkey which formed the bridge over which plague travelled from Asia to reach Europe.

In Asia plague, like cholera, has its *endemic centres*, starting from which it spreads in an epidemic form at longer or shorter intervals. It cannot, however, be conclusively stated which country is to be regarded as the actual home of plague. Certain facts, however, point to the probability that the disease has its seat in *Southern Thibet*, on the *northern declivity of the Himalayas*. The source of the epidemics in India and South China may presumably be sought for in this locality.

Plague has been known in *India* for a very long time. Even in one of the Parânas,[1] which is at least eight hundred years old, instruction is given to leave the place as soon as an epidemic is observed among the rats—an order which undoubtedly refers to plague. From time to time the country has been visited by epidemics of plague, which sometimes spread over a larger or smaller area, and sometimes occurred simultaneously with the great European epidemics ; sometimes, on the contrary, the disease had only a small circumscribed area of extension, being limited to the provinces of Kumaon and Gurhwal, situated on the south-western declivities of the Himalayas ; for the disease known here by the natives as *Mahamari* is identical with plague.

It is probable that plague was introduced from Thibet into the adjacent *Chinese Province of Yunnan*, where it developed in the valleys. This centre, to which attention was first directed in 1878 by Rocher, an official employed in the service of the Imperial Maritime Customs of China, has its centre in the town of Mengtsz, and has lately attained great importance, for it undoubtedly formed the point of departure of the present great pandemic of plague. The disease exhibited itself repeatedly in Lien-tschau

[1] A number of comprehensive poems containing theological and philosophical teachings, ritual writings and legends, are in the literature of Hindostan called Parânas.

and Pakhoi on the Gulf of Tongking, afterwards spreading from the latter to Kwang-tung in March, 1894 ; in May of the same year it attacked Hong Kong and Canton, and later was transmitted to Amoy. In 1895, Swatow, Foochow, Macao, and many other places in South China were attacked, and in the following year the disease re-appeared on the coast of China and spread to the island of Formosa. In August, 1896, the plague suddenly broke out in Bombay. Probably the introduction of the disease was effected by means of the maritime commerce from the Chinese ports ; it is asserted, on the other hand, that it was spread from the hinterland by the pilgrims from North India (Kumaon and Gurhwal), where in 1893 and 1894 outbreaks of Mahamari had been reported.

From Bombay the disease gradually spread over a large portion of the Indian peninsula, and has retained a firm footing there up to the present day, with only periodical and local undulations. From the autumn of 1896 to January, 1899, about a quarter of a million persons succumbed to the plague. Nor was the disease limited to China and India. Off-shoots of the China-Indian epidemic spread to Madagascar, Mauritius, Réunion, Mozambique, Delagoa Bay, the Philippines (Manila), Japan, the Sandwich Islands, New Caledonia, Australia (Adelaide, Sydney), Djeddah, Suez, Alexandria, and even to Europe and America. Isolated cases have repeatedly been brought to European ports (London, Plymouth, Trieste), nevertheless without bringing further cases in their wake, and in June, 1899, an epidemic broke out in Oporto. Quite lately plague even made its appearance in Paraguay (Asuncion), Brazil (Santos, Sao Paulo, Rio de Janeiro) and Argentina (Rosario). This is the first time on record that plague has shown itself in the New World. The old opinion, moreover, that plague is unable to pass the equator, has been quite upset by the present epidemic, and it is impossible to foresee in what direction, and how far, it still may wander.

Matignon reports that since 1888 plague occurs every year with more or less virulence in the valley of So-leu-ko in North China, on the borders of Mongolia, but it is not known how and by what way it was first imported there.

A second centre of plague, and one long known, is situated in Mesopotamia, and to this centre the epidemics frequently occurring in Persia, more particularly in the province of Azerbijan, may be traced back, and there is also probably some connection between this centre and the epidemic in Wetljanka (Astrachan) mentioned above, as also with the outbreaks of plague occurring near Samarcand (Russian Turkestan) in 1898, and in Kolobowka (mouth of the Volga) in 1899.

A third plague centre exists in the mountainous district of *Assir* on the *west coast of Arabia*, but as yet it has attained no great importance, as widespread epidemics have not originated there.

We are indebted to Robert Koch for our knowledge of a fourth endemic centre in the *interior of Africa*, probably in *Uganda*. Koch, in common with Zubitza, established the fact that the disease, which for some years has prevailed in Kisiba, the extreme north-west of German East Africa, and which is by the natives called " *Rubwunga*," is identical with plague. The disease, which has been endemic in Uganda for ages, was undoubtedly carried thence to Kisiba. This centre is undoubtedly the source of the former epidemics in Egypt and the other countries on the north coast of Africa, and was carried principally through the importation of slaves. Egypt has for ages been frequently afflicted by epidemics of plague, of which the last one—apart from the recent outbreak in Alexandria—occurred in 1844 ; while in Tripoli, in the district

of Benghasi, various epidemics, the origin of which was hitherto shrouded in mystery, broke out in 1856-59 and in 1874. This African plague centre may attain overwhelming importance on completion of the railway now in course of construction between Mombasa in British East Africa and Uganda.

There is probably still another plague centre in East Siberia, in the steppe-regions of the military district Akscha in the Trans-Balkan province. The Russian doctors, Bieliavsky and Reschetnikoff, report a disease occurring there, the clinical description of which, above all the appearance of buboes, speaks for its identity with plague (Favre). It is to be hoped that bacteriological examinations will elucidate the nature of the outbreak.

ETIOLOGY.

Plague is originated by a specific micro-organism which was discovered in Hong Kong in 1894 by Kitasato and Yersin simultaneously and independently, and the correctness of which discovery has been fully confirmed by the respective commissions for investigation of the plague sent from Germany, Austria, Russia, &c. A most striking and sad confirmation of the discovery was yielded during the laboratory experiments in Vienna in 1898, the origin of which was traced to the cultures of the microbe brought from Bombay, and which caused the loss of life of three persons.

The specific factor in plague (see fig. 1, plate I.) is a short, thick *bacillus*, endowed with very slight or no movement, the ends are rounded off, and it shows some similarity to the bacillus of chicken cholera. It is easily stained with aniline dyes—weak, watery solutions of methylene blue or much-diluted Ziehl's solution are particularly suitable—but not by Gram's method; the ends take the stain more easily than the middle. The bacillus exhibits great variability in form and size, every transition occurring, from short, almost spherical, bacteria to extended rodlets. It is surrounded by a mucoid cortex which, however, it is not easy to demonstrate. It is usually found presenting the appearance of a diplobacillus, but is also sometimes seen united in short chains. Spores have not been observed.

The plague bacillus, according to Bitter, appertains to the *septicæmic microbes*, inasmuch as in animals of very great susceptibility it passes directly into the blood without any visible local reaction taking place. Microbes in those with less susceptibility, on the other hand, cause a local reaction, and only generate septicæmia in fatal cases ; of these the anthrax bacillus is a typical example. Plague, however, takes a unique position amongst septicæmic diseases, inasmuch as, unlike the others, the local reaction sets in, not on the place of inoculation, but in the corresponding lymphatic glands.

The plague bacillus, in the first place, is found in the *buboes* which represent the primary seat of the disease, and to which, in slight cases, it remains restricted. When streak preparations of bubo-juice are made one sees in typical cases—besides pus corpuscles, cellular detritus, and numerous red blood corpuscles originating from hæmorrhages—such vast numbers of the bacteria that the contents of the bubo seem to consist of these only. In preparations of sections of buboes also, in which the bacilli lie partly in the gland cells and partly in the lymph spaces, their number, as compared with the number of the gland cells, is positively overwhelming (Kolle). When the buboes begin to suppurate, the bacilli rapidly disappear.

Besides being present in the glands, the bacilli, in serious cases, are found in the *blood* and in *all the interior* organs, especially the *spleen*, but seldom earlier than twenty-four hours before death. Their number in the blood vary considerably, being sometimes so sparse that several preparations have to be examined in order to discover them. The bacilli have also been found in the bile, urine, sputum, saliva, coating of the tongue, and in primary skin lesions (pustules, carbuncles, &c.); they have likewise been found in the fæces by Kitasato and Wilm.

The plague bacillus can be *cultivated* on the usual bacteriological nutritive media, provided these are tolerably concentrated; the growth, however, is very slow. It thrives within a wide range of temperature. It develops almost equally well between 37°[1] and (about) 25°; it grows at between 10° and 15°, though more slowly, and even at 5° (refrigerator temperature). These qualities are invaluable for isolation of the plague bacillus from mixed bacteria.

On *gelatine* which is not liquefied, there forms in two or three days at 22° fine semi-transparent dots, which, if on the surface, consist of hemispherical prominences of a yellow or yellowish-brown colour; these are not sharply defined, but are surrounded by delicate, pellucid borders of bacilli indented at the edges (German Commission).

On *agar-agar*, at incubation heat, there develops a whitish, fairly thick aggregation which, on being touched with a platinum wire, exhibits a peculiar sticky, slimy consistency, and does not cling tightly to the under surface (German Commission). Haffkine was the first to draw attention to the fact that, in old, particularly in dried up agar-agar cultures, there develop large, peculiar involuted forms, inflated, spherical, fusiform, oval and pear-shaped. If 2·5 to 3·5 per cent. of salt be added, the same involuted forms appear, as proved by Hankin and Leumann, develop at 37° after twenty-four hours, a fact which is of importance in differentiating these from allied bacilli.

When the plague bacillus is cultivated in *bouillon*, the medium slowly becomes turbid, and after a few days there appears at the bottom of the glass a white flaky deposit, which gradually increases in quantity. If kept perfectly quiet a white ring of vegetation forms simultaneously on the upper edge of the layer of bouillon clinging to the glass, and extending slowly till it is a thin floating membrane on the surface of the bouillon (German Commission). If a few drops of melted butter (ghee) or cocoa-nut oil be poured on the culture, the bacilli grow down from the surface into the fluid in the form of long filaments which resemble stalactites (Haffkine). In very old cultures the turbidity gradually diminishes until the fluid may again become quite clear.

According to the investigations of the German Commission the plague bacillus cannot thrive if atmospheric oxygen be withheld; according to Abel, however, its development is equally good aërobically and anaërobically.

In *saccharine* substrata, no fermentation accompanied by gaseous formation is originated by the bacillus.

Plague-like disease can be produced in animals by means of *inoculations* with cultures, and also by the juice of buboes and sections of the organs of plague cadavers. As to the susceptibility of the various species of animals, the conditions are, according to the experiments of the German Commission, as follows:—Birds and pigs are refractory; cats and dogs exhibit a weak reaction; sheep, goats, cows and horses a strong reaction. Monkeys, and all rodents in particular, are highly susceptible. Rats possess the greatest predisposition of all animals, and may be fatally infected by way of the intact mucous membranes and the digestive tracts. To produce such an infection it suffices to touch the ocular conjunctiva, or the nasal mucous membrane with culture substance, or to feed the animal with the smallest quantity of culture. The gnawing of the bodies of their companions who have died of the plague, as rats are known to do, likewise causes infection.

In rats and mice also plague likewise occurs under natural circum-

[1] All temperatures given in this book are according to Centigrade scale.

stances, an observation which had already been made in the epidemics
of former centuries, but which was particularly noted recently on the
occasion of the Chinese and Indian epidemics. In Canton the seizure
of human beings was preceded for two or three weeks by wholesale mor-
tality amongst rats ; these left their holes in shoals, staggered about over
each other, finally falling down dead, and this occurrence was repeated
in every newly plague-infected part of the town. According to Janson,
in one division of the town alone more than 35,000 dead rats were
collected. This observation, so frequently made, has led to the opinion
that plague is really *a primary disease of rats*, and is first transmitted
from them to man. It has been asserted that other animals, such as
pigs, dogs, jackals and snakes sicken spontaneously with plague, being
infected by having devoured diseased or dead rats, or human plague
cadavers, but this statement requires further investigation for confirma-
tion.[1] In Hardwar (India) plague is also supposed to have affected
monkeys which had taken possession of deserted plague-stricken dwellings.

The plague bacillus has been but seldom found outside human and animal organisms,
although it has been discovered a few times in dust, sweepings, and water contaminated
with fæces (Kitasato, Wilm, Hankin, Leumann).

Outside the body the plague bacillus possesses a relatively slight
capacity for resistance. It soon perishes in water, and it is rapidly
destroyed by disinfectants, by being heated, and by sunlight. The
bacillus is also very sensitive to desiccation, when rapidly carried out—
as by means of a high temperature or in the exsiccator—whereas slow
drying up at a low temperature is less harmful. Therefore if dried up
in a tropical climate it perishes much more rapidly than in a temperate
climate. Pure cultures, protected from light and desiccation, preserve
their power of development for months. It follows, therefore, that the
bacilli may preserve their capacity for development in dark and damp
places ; and as, as mentioned above they thrive even at a very low tem-
perature on the most different nutritive media, and even possess a remark-
able capacity for resisting frost, it is possible that in our climate also
they may remain alive and multiply outside human beings and animals.

Investigations conducted as to the power of resistance of the plague bacillus by
different observers vary considerably one from the other. This is at least partly due to
the differences of the climates in which the observations took place, and by the different
methods of experiment. It may also be explained by the fact that cultures of different
origin as they exhibit distinction in their virulence (Kolle) also exhibit a difference in
their power of resistance. According to the investigations of the German Commission,
the bacillus is killed by heating to 70° in ten minutes, by heating to 80° in five minutes,
by 1 in 1,000 sublimate immediately, by 1 per cent. carbolic acid in ten minutes, by
5 and $2\frac{1}{2}$ per cent. carbolic acid in one minute, by 1 per cent. lysol in 5 minutes, by 3 per
cent. of soft soap in thirty minutes, by 1 per cent. chlorinated lime in fifteen minutes,
and by 1 per cent. solution of quick lime in thirty minutes. Furthermore, the plague
bacillus is very sensitive to mineral acids : sulphuric acid 1 in 2,000 kills it in five minutes,
and hydrochloric acid 1 in 1,000, in thirty minutes. Exposed to direct sunlight it dies
off within an hour, drying up to a very thin layer on the cover glass. Dried up and
preserved in the most varying conditions (in sections of organs, in clothing, in the soil)
the bacillus in India never exhibited life longer than eight days, whereas in a European
climate it resists desiccation longer (according to Abel's investigations in Greifswald,
fourteen days and even longer). Deposited in the ordinary water from the main it lasts
at the longest five days, in sterile water ten days, and in sterile fæces and urine it is
dead after five days. It endures a long time in sputum, being still infectious on the
tenth day, but not so on the sixteenth. Low degrees of temperature are borne remark-

[1] According to a report by Locans (*Brit. Med. Journ.*, December 2, 1899, p. 1,588),
plague was also observed in cats (cervical buboes with bacilli) in Mauritius.

ably well by the plague bacillus. Kasansky found cultures viable after being exposed to the cold of winter for five months at a temperature of 31°, during four months of which time they were completely frozen through.

Aoyama first called attention to the fact that, besides plague bacilli in the lymphatic glands, blood and viscera, various other bacteria are found, such as *cocci, streptococci, staphylococci, bacterium coli, diplococcus pneumoniæ,* so that there is a *mixed infection* which may originate from ulcerated tonsils, pneumonic centres of the lung and buboes without or after surgical interference. The suppuration of the glands is to be attributed to the appearance of suppurative agents, and after the appearance of the latter the bacilli disappear. Sticker always found staphylococci and streptococci when actual abscess formation had set in; but these microbes were never confirmed when there was only puriform breaking down of the bubo with initial liquefaction of the same and subsequent absorption, or artificial evacuation of the chocolate-coloured contents. Carbuncles, according to Bitter, are probably originated by a mixed infection; this author was unable to find bacilli in carbuncles.

The bacilli of plague most frequently gain entrance to the body through the *skin* or the *mucous membranes* near the facial orifices. When the skin is intact it is possible that the bacilli may gain the lymph passages through the orifices of the sebaceous glands. According to the statements of the Austrian Commission, animals can be infected by cultures being rubbed upon the unshaven skin. In the majority of cases, however, the point of entrance is undoubtedly at the seat of small *injuries,* such as bites of insects, scratches and so on, to which dirty bare-footed natives, covered with vermin, are particularly liable. It is remarkable, however, that in Europeans who wear foot-gear, inguinal gland affections are most frequent; thus proving that the inoculation takes place by way of the lower extremities, although they are exposed to less injuries than the hands. It would therefore seem as though the region of the inguinal glands is the *locus prædilectionis* for the development of the plague bacilli in the body.

The point of entrance at the time of the illness is no longer visible, because during the period of incubation the small lesions heal, and as a rule no local reaction sets in at the seat of infection. It is only quite exceptionally that the point of entrance is observable as small papules, blisters, or pustules, containing bacilli. In consequence of infection taking place at autopsies plague has often been transmitted to doctors and their attendants.

The *respiratory organs* form another point of entrance for the bacilli. Plague-pneumonia is doubtless to be traced to infection by inhalation, but, as the plague bacilli have no capacity for resisting desiccation, the transmission must take place less by way of the dried bacillus in dust than by the tiny drops of sputum containing bacilli diffused by plague patients when speaking, coughing and sneezing (*Flügge's drop infection*).

In one small series of cases the infection, according to the Austrian Commission, originates from the *tonsils.*

The *gastro-intestinal canal* is, finally, according to Wilm's investigations, a fourth way by which the bacillus of disease may be received into the body. The transmission takes place through eating infected food (according to Janson by partaking of the flesh of plague-sick pigs) or drinking infected water. Wilm also found, in contradistinction to the results of the investigations of the German Commission, that the bacilli were still viable for two days in ½ per cent. solution of hydrochloric

acid, and he even confirmed their presence in the water of an open well that was exposed to contamination. Though Wilm's observations have not been confirmed by others, his opinions are supported by the fact that plague can be experimentally induced in animals by this method of infection (Bandi and Stagnitta-Balistreri), and that the mortality amongst rats is largely due to typical intestinal plague.

The *period of incubation* fluctuates between thirty-six hours and ten days, the average being four to six days. Exceptionally it may extend longer, even to twenty days.

The *spread* of the disease takes place by means of *persons, animals* and *inanimate objects.*

In regard to the first method of transmission, a great deal depends on the form of illness exhibited. Cases belonging to the simple bubonic form play a very unimportant part; the bacilli, in this form, are already imprisoned in the buboes, and when these suppurate and burst open the bacilli have mostly already perished. Septicæmic cases, on the other hand, are very important; for in these, during the last stage of the disease, the bacilli are in the blood, and may escape thence by way of the numerous internal and external hæmorrhages, and may therefore find an outlet by means of the vomit, stool, urine, sputum, &c. The pneumonic form, however, is the most dangerous of all for the bacilli may be easily disseminated through the expectoration.

That the danger of contagion is much lessened by cleanliness is proved by the rarity of infections in the staffs of well-kept hospitals.

Animals, above all, as already mentioned, *rats,* are greatly implicated in the spread of plague. As was confirmed by the German Commission, myriads of virulent bacilli are evacuated by plague-stricken rats in their urine and fæces, and human beings may come into contact, directly or indirectly, with the same and thus become infected. Rats play an important part in the spread of the plague on board ship. Simond communicates an instructive example of this: a ship left Bombay at the time of the epidemic, after having been thoroughly disinfected, and arrived at Aden without a case of illness having occurred on board. On the return voyage from Aden dead rats were found in the postal cabin, and soon after the postal official, taken on board at Aden, fell ill of plague.

Besides rats, *insects* also (flies, mosquitoes, fleas, bugs, lice, ants and beetles) come under consideration, for all these are intermediary carriers between rats and man, and may also have the same effect between man and man. Bacilli were detected in flies which had died in Yersin's laboratory; they have also been found in fleas on dead rats and in ants which had fed on dead rats. It is by no means necessary that the bacilli of the infected insect should be directly inoculated to cause the transmission; it suffices that the bacilli, on or within the infected insect, escape whilst the insect stings or when it is by chance crushed on the body or trodden on, and gain entrance by small superficial wounds. Hankin and Simond succeeded in experimentally transmitting the disease to rats and mice through infected insects, whereas Nuttall's experiments in this direction had negative results.

From certain facts observed it appears that plague may be spread by means of inanimate objects, by articles used by plague patients, such as linen, clothes, bedding, &c.; it can also be disseminated by merchandise. These facts are likewise proofs that the plague bacilli, under favourable conditions, possess a far greater power of resistance than one is led to expect from experiments made in the laboratory. As an instance, corn sacks may form a means of infection by having harboured diseased rats which had made their way into granaries and there died.

A striking example of the *transmission of plague by means of infected clothes* has been mentioned by Hirsch from the epidemic in Wetjlanka, 1878-1879. It relates to a little girl aged 10, into whose parents' house a trunk of clothes had been brought from a house in which, about two months previously, all the inmates had succumbed to plague. The girl opened the trunk, which had hitherto remained untouched and which was destined to be burned, took an article of clothing out with which she played, and four days later the first symptoms of plague set in at a time when the epidemic of Wetjlanka had already disappeared. The plague was brought to Oporto not by persons but by goods, this being proved by the fact that the first five patients were Spanish labourers in the dock who were employed in shipping and unshipping the goods (Hauser).

When plague has been carried into a place the spread is very slow. From the time of introduction until the appearance of the first local case weeks and months may elapse. In two examples from India, quoted by the Egyptian Commission, the period was eighty-six or eighty-seven days. The first cases of the disease group round the imported case and affect members of his family, or persons who have become infected by nursing and visiting the case. In such instances it is undoubtedly a question of direct transmission from man to man. There then follow some sporadic cases in neighbouring houses, and then also in distant quarters of the town and in persons amongst whom direct communication with the first patients cannot be proved, and which are only explicable as having been transmitted by the agency of rats. Thus the epidemic spreads slowly in the course of weeks and months, till it finally attains its highest point when, as a rule, it decreases as slowly as it had first increased and dies out, or it may drag on with fluctuations for years. During the epidemics in Bombay and in Hong Kong, plague infection seemed to cling pertinaciously to certain localities. In some houses the inmates all succumbed to the disease, whilst in adjacent houses the people were altogether free or but slightly affected with plague.

In explanation of this phenomenon, also, the rats probably play their part. After the subsidence of an epidemic, sporadic cases occur, sometimes for years, and sometimes, even, there is a recurrence of the plague without a new introduction having taken place. It is probable that the illness has been maintained in the interim by rats. The same is probably the case also in the districts in which plague is endemic, epidemics developing from the sporadic cases from time to time. Probably in endemic centres of rat-plague a certain immunity to the disease is engendered amongst the rats as the disease passes and re-passes from animal to animal. One may imagine, also, that the rats spread the disease during the course of their travels, which are undertaken in consequence of unusual phenomena of nature, such as floods, earthquakes, &c. They thus carry plague into healthy regions, the non-immune rats of the locality acquiring the disease in the severe form and dying wholesale.

Probably other animals also are responsible for the maintenance of the plague germ. The above-mentioned plague-like disease (see p. 6) in East Siberia is traced to a rodent related to the marmot, the arctomys bobac (the tarbagan),[1] which inhabits the high mountains, and is also found in the Himalayas. There rages amongst these animals a disease known amongst the natives as "arctomys-plague," and which is transferred from sick or dead animals to man by contact, and is then further spread by the latter by contagion.

Seasons and *atmospheric temperature* exercise a certain, but not very important influence on the origin and spread of a plague epidemic. Moderate warmth, in conjunction with moisture, seems the most favour-

[1] See *Journal Trop. Med.*, Clemow, February, 1900.

able atmosphere for the development of the plague germ. In the cooler regions of the East, and formerly in Europe, the epidemics usually occurred in the summer. In Central Egypt, particularly in Cairo, the epidemics were apt to subside at the height of the summer, during the prevalence of intensely dry heat, epidemic outbreaks never starting at this period of the year. In Mesopotamia, plague principally appeared during the coolest weather and practically ceased during the hottest season. In India, also, it is markedly during the cooler months that plague prevails. In most of our cities, as, for instance, in Bombay, the height of the epidemic occurs in the "winter." In a few towns, however, the opposite observation was made. It is certain that the meteorological conditions alone do not in this respect come into account, but exercise their influence on the manner of living of the population. Whereas the natives during the hot season mostly pass the night in the open air, they in the cooler season, being very sensitive to cold, not only retire into their dwellings by night but wrap themselves up in bedding and covers, and close up every aperture to keep out the cool night air. It stands to reason that these proceedings have a favourable influence on the spread of the plague germ. In Hong Kong, according to Wilm, the plague in 1894 and 1899 raged during the hot months ; in 1896, on the contrary, it raged during the cooler season and stopped suddenly when the hot weather set in. Taking into consideration the power of resistance the plague bacillus exhibits to frost, it is not surprising that epidemics have been observed during the severest winter weather (in Moscow in 1771 and in Astrachan 1878-1879).

Neither the *geological character of the soil* nor a high elevation above sea level has any influence on the occurrence of the disease. In India plague has been observed at a height of over 10,000 feet.

On the other hand the development and spread of plague is influenced in a great measure by the *unfavourable hygienic conditions, essentially connected with social misery.* Agglomeration of dirt in the houses and in the streets, defective removal of fæcal and other animal excretory matter, crowding and insufficient ventilation of the dwellings, bad and insufficient food, &c., all help as predisposing causes of illness. The poorer part of the population are always stricken most heavily, occasionally also they are the only victims. It was on this account that Cabiadis designated the plague "*miseriæ morbus.*" If amongst the population of a town or country the peoples of different races and nationalities are attacked in an unequal degree, this is attributable less to the racial difference than to the different hygienic conditions under which they live. In Canton, during the epidemic of 1894, the foreigners with their native servants living in good hygienic surroundings on the Island of Shamien were completely free of plague, while many Chinese dwellings on the opposite side of a branch of a river 50 feet wide, which separates the island from the town,[1] were attacked by the disease. In Hong Kong, according to Ayres and Lowson, the well-housed, clean Europeans were rarely attacked, whilst the Chinese, living in notoriously unsanitary environment, were most seriously afflicted. In regard to mortality, the Japanese, Portuguese, Manila folksand Indians took a position between the Europeans and Chinese. In Bombay the Europeans and Parsees suffered least, the Mohammedans and Hindoos most, whilst the Jains (Hindoo caste) and Jews took the position between.

The increase in cleanliness and the improvement of public and private

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[1] *Brit. Med. Journ.*, September 15, 1894, p. 615.

hygiene have decidedly played an essential part in the disappearance of plague from Europe.

Sex exercises no predisposing influence. Both sexes are equally attacked. When pregnant women are taken ill they usually miscarry and die.

Age appears to determine in some degree the onset of plague ; persons between the ages of 20 and 30 years are most frequently attacked ; infants at the breast very rarely contract plague. Leumann reports one case of intrauterine transmission.

The child of a plague patient, born at term, fell ill ten days after birth with buboes in both axillæ and groins, and died after an illness of eighteen hours. At the autopsy bacilli were found in the blood, spleen and lymphatic glands.

Occupation seems to play but a small part in predisposing to plague. According to the older observations, persons who have much to do with water, such as water-carriers, bath attendants, &c., enjoy a remarkable immunity, as do also, but to a still higher degree, oil and grease dealers. This immunity may perhaps be explained by the fact that people engaged in occupations of the kind are freer from vermin. The reports of later epidemics, however, do not support this theory. In Bombay, barbers, servants, jockeys, grooms, washermen, agricultural labourers, artisans, spinners and weavers, corn and flour dealers, bakers and fruiterers were, in particular, most severely attacked (German Commission). According to Yamagiwa, those persons especially who have to do manual labour, and those whose occupations lay them open to injuries, are most liable to be attacked by plague.

The predisposition to the disease is not always extinguished by once having had the same. A second attack of the same individual has occasionally, even in the same epidemic, been observed. Sometimes only a few weeks elapse between the first and second illness. The second attack mostly has a fatal termination.

The causes usually assigned as determining the onset of ailments, such as chills, mental and bodily exertions, errors in diet, fright, fear of the disease, previous illnesses, &c., are all regarded as playing a part in the initial development of the illness.

SYMPTOMATOLOGY.

Plague may cause signs and symptoms of so diverse characters that several forms of the disease are now differentiated. Of these the most frequent and most typical is bubonic plague.

1. Bubonic Plague.

The outbreak of the actual disease is but rarely preceded by *prodromal* symptoms, which, when present, consist of indisposition, languor, depression, slight chilliness, stiffness, pains in the limbs, headache, insomnia, loss of appetite, nausea, vomiting, palpitation, sometimes also dull aching in the regions of the groins and armpits, which at a later period become the seat of the buboes.

In most cases the *onset of the illness* is *sudden*, with high fever which is sometimes, but not always, ushered in by one or more rigors, and, in the case of little children, by convulsions ; it is accompanied by very severe constitutional disturbances, and pronounced bodily and mental weakness.

Pain and enlargement in some group of glands generally accompany the initial development of fever, or they may appear, according to Lowson, somewhat later—on the second day as a rule. It is also noticeable that in many instances the bubo even precedes the rigor. In addition there is headache usually localised in the frontal or temporal region; giddiness which may increase to severe delirium; loss of appetite; at the commencement there is sometimes nausea and vomiting, occasionally, also, diarrhœa, pains in the epigastrium, and aching in the back and limbs. Oppression and drowsiness, or, on the contrary, restlessness and a feeling of anguish and sleeplessness obtain. The speech becomes thick, the gait tottering, so that the patient conveys the impression of a person severely intoxicated. Soon stupor sets in, accompanied by a quiet passive condition of mind, or, more rarely, wild delirium develops. In severe cases the patients already, on the second or third day, exhibit a pronounced typhoid state, with deep prostration, accompanied by muscular twitchings, and also tonic and clonic spasms. Sometimes, on the other hand, the brain remains perfectly clear until death.

The *type* of *fever* in plague is more or less markedly of a continued or remittent type. The temperature mostly rises rapidly, and either on the first, but more frequently on the second day, its highest point—often 40·5° to 41°—is attained. More rarely the rise of temperature takes place gradually. On the third or fourth day it sometimes goes down 1°, 1½°, or more, and in slight cases it may fall to normal.

Generally, however, the temperature rises again, seldom, however, to its former height, and then between the fifth and seventh day it suddenly sinks to normal or subnormal. Often the temperature rises again and a remittent suppurative fever, due to a secondary invasion of streptococci, sets in. The attack of a fresh gland or group of glands is followed by a renewed rise of temperature, and complications, such as secondary pneumonia, may cause undulations of the fever curve. The temperature rises before death in many cases, and the accompanying charts, borrowed from the reports of the German Commission, may serve as an illustration of this statement (figs. 2 to 5).

The *pulse*, as a rule, is at first full and dicrotic, later very small, and but rarely irregular and unequal. The number of beats mostly averages 120, being seldom below 100, but many rise to even 140, 160, or more per minute.

The *respiration* also is accelerated to from 30 to 40 respirations per minute.

The *skin* feels burning, hot and dry until the third or fourth day, when should the temperature fall it becomes moist. When the afebrile period sets in there is almost always perspiration, which is maintained for a day or two, more particularly at night.

The *patient's* face at the commencement of the illness is mostly reddened and somewhat puffy; the expression is dull, often anxious; the eyes are sunken and glistening, the look staring, the conjunctivæ are more or less injected.

The *tongue* is at first swollen and moist, and exhibits a white coating which has been compared to chalk or mother-o'-pearl. Later on the tongue becomes dry and fissured, and, in addition, the teeth, the lips, and the nostrils are covered with dark crusts. The *tonsils* are occasionally swollen, and the pharynx, as a rule, appears dark red.

In the later stages of the disease a diphtheroid pharyngitis has been noted—a condition which is to be regarded as of the gravest significance (Müller).

The *heart,* at an early stage of plague, shows signs of dilatation, and murmurs are frequently heard at the apex or over the pulmonary artery.

As to the *blood,* the red blood-corpuscles are often considerably diminished, and moderate leucocytosis is present.

The *abdomen* is sometimes distended; the spleen enlarges at an early stage of the disease—on the second or third day—but it seldom extends beyond the costal margin by more than a few centimetres; the liver also enlarges to a slight extent as a rule.

The secretion of *urine* is diminished, and occasionally quite suppressed. Aoyama and Bitter often observed retention of urine, so much so that the catheter had to be used. The urine is dark, with a strong acid reaction, exhibits a high specific gravity and deposits urates; it frequently contains albumen (nucleo-albumin and serum-albumin) but always under $\frac{1}{2}$ per cent. (Austrian Commission); it but rarely contains blood. Examined microscopically the urine is frequently seen to contain granular, a few hyaline casts, white and red blood corpuscles, but fatty casts are seldom observed. The Austrian Commission observed, in nearly all cases, a considerable decrease of chlorides.

Buboes are the most characteristic signs of plague. The glands attacked become rapidly enlarged, and may attain the size of an apple, or fist, and may attain even larger dimensions. The pain increases with the enlargement, and is often so great that the patients groan and wail; at other times, however, there is but slight pain, and then only when pressure is made on the glands. The buboes most frequently develop in *the inguinal region,* but extend downwards into Scarpa's triangle. Next
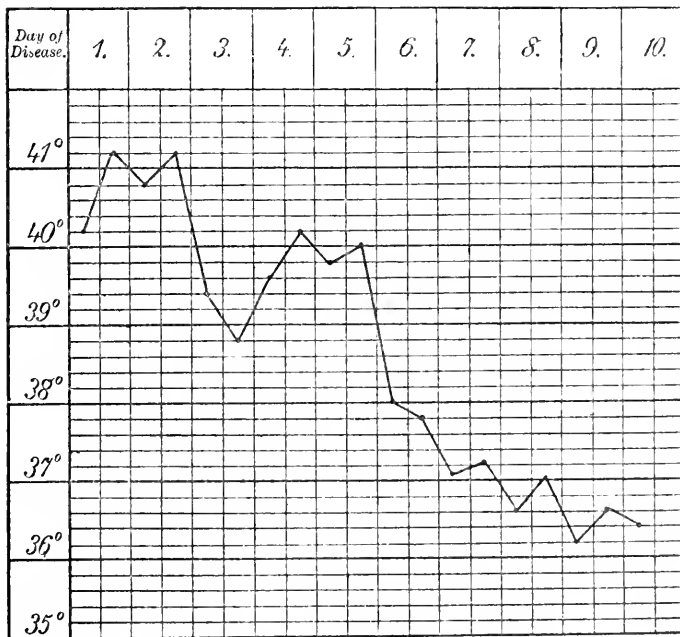
FIG. 2. —Bubonic plague; incision of the buboes. Recovery.
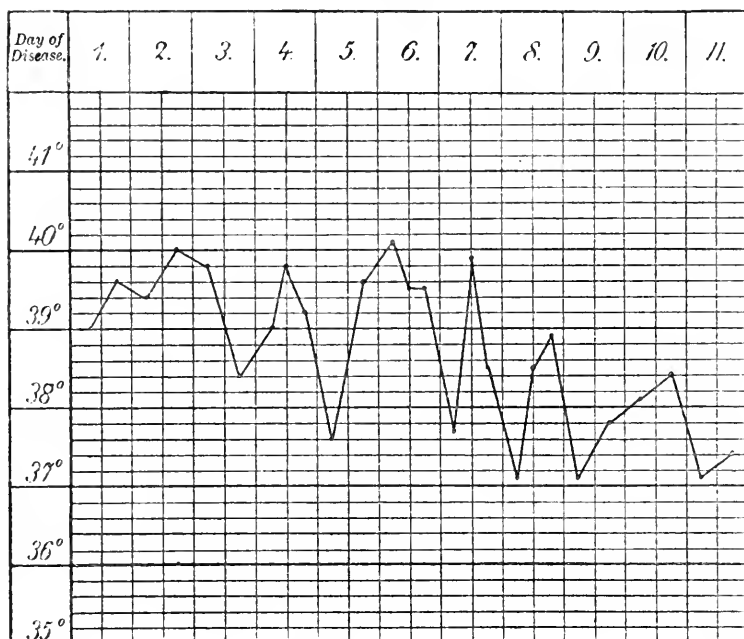
FIG. 3. —Bubonic plague with carbuncle.   Suppurative fever.   Recovery.
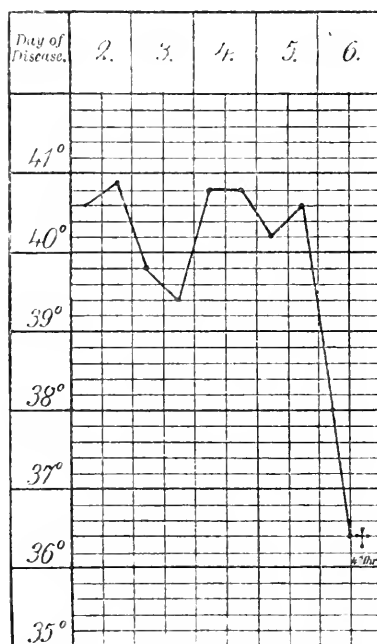
FIG. 4.—Bubonic plague.   Sepsis.   Death.
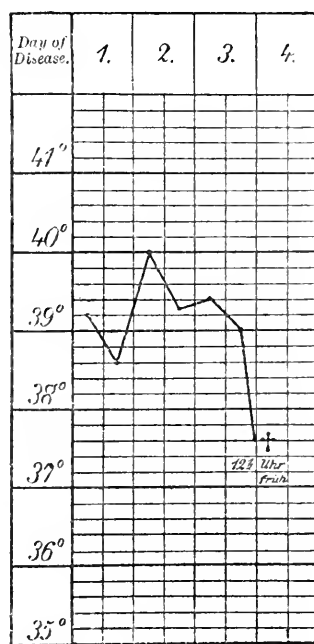
FIG. 5.—Pneumonic plague.   Death.

in frequency buboes develop in the *axillary region*, where, as in the groin, the deepest seated glands are primarily affected. Next in frequency come the glands at the *angle of the lower jaw* and *neck*. The glands of the elbow and the popliteal space are very rarely affected. Any peripheral lymphatic gland may, however, become the primary seat of infection. The submaxillary glands are in children most frequently attacked, owing no doubt to the habit children have of putting all sorts of things in the mouth. When axillary gland buboes are present the supraclavicular glands are also more or less affected.

The following statistics are by Russell, and relate to 2,700 cases of plague. Of this number 1,841 were inguinal, 569 axillary, and 231 submaxillary buboes. Inguinal buboes occurred 175 times on both sides, 729 times on the right side only, and 589 on the left side only. Submaxillary buboes were only observed 130 times, and of these 67 were on children. Cabiadis amongst 1,826 children observed 710 inguinal, 406 axillary, 98 cervical, and 122 buboes at several regions simultaneously. Of 300 patients treated by Wilm in Hong Kong, 219 (that is to say 73 per cent.) had buboes, and of these 128 (42·6 per cent.) had one-sided inguinal or femoral buboes, 10 (3·3 per cent.) had double-sided femoral buboes; 33 (11 per cent.) had axillary buboes one side, none on both sides; 32 (10·7 per cent.) had cervical buboes on one side, 3 (1 per cent.) had cervical buboes on both sides; 3 (1 per cent.) had submaxillary buboes on one side, none on both sides; 2 (0·7 per cent.) had one-sided buboes at elbow, 8 (2·7 per cent.) buboes on various parts of the body; 81 (27 per cent.) were cases without marked buboes, but having on one or more places of the body painless, or more or less painful, glands generally enlarged to the size of a hazel-nut.

The symptoms which indicate *internal buboes* are oppression, pains in the depth of the abdomen, and pains in the lumbar region.

According to the statements of the German Commission the *lymphatic apparatus* of the *mucous membranes* may be attacked. Of these there came under observation buboes of the tonsils, as also primary ulceration of these with secondary buboes at the submaxillary angles, and in one case buboes of the glands adjacent to the hyoid bone.

Usually only one group of glands becomes affected, more rarely several. In the latter case these do not usually all become affected at the same time, but one after the other. The glands of a group do not all enlarge in the same degree; one may attain the size of a hen's egg, another may only become as large as an almond, while the others do not become at all enlarged, and are scarcely palpable. There is no agreement between the development of the buboes and the severity of the general symptoms. As a rule inflammation of the periglandular tissue and of the skin soon accompanies the glandular enlargements; the glands then can no longer be felt separately, nor can they be felt to be movable beneath the skin. A smooth, painful infiltration ensues, over which the skin is reddened and becomes œdematous.

The buboes may become absorbed, they may leave an induration and thickening of the glands, but more frequently they *suppurate*. According to Wilm's observations made in Hong Kong in 1896, suppuration takes place in 90 per cent. of the cases. Absorption takes place in mild cases, and suppuration in mild cases as well as in severe. The abscesses generally come to maturity during the course of the second week. Sometimes the suppuration is prolonged for weeks, one gland after the other forming into abscesses. Phlegmonous changes and gangrene may supervene at the seat of suppuration.

Those cases with buboes in the cervical and submaxillary glands exhibit the most severe evidence of the disease, for the plague bacilli, or their products, from the glands in nearer proximity to the centre of circulation, invade the blood stream far more quickly than those further

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distant (Yamagiwa) ; and besides this, the mechanical effect of the dense infiltration of the surrounding parts, with compression of the trachea and œdema of the glottis, add to the severity of the infection (Austrian Commission).

Pustules, boils, and *carbuncles* are observed far more rarely than buboes, and may be more frequent during one epidemic than in others. They are apt to appear between the first and seventh day of disease. A brown spot the size of a lentil may form on any part, most frequently the extremities. Its appearance is heralded by a feeling of heat and pricking or itching pains. The skin surrounding the lesion becomes bright red and indurated. A small blister develops over the spot with opaque contents and dark red border ; the swelling increases in size and may attain the dimensions of a hazel nut. The base of the blister necroses and forms a black scab. After this has been removed by suppuration a black, crater-like ulceration with a dry base appears, which may finally cicatrise. But on the other hand inflammatory changes may lead to widespread necrosis, whereby wide areas of muscle are laid bare, and severe hæmorrhages may result.

Plague boils are either *primary or secondary.* In the former case they sometimes constitute the first focus of the infection, and a glandular swelling appertaining thereto appears secondarily. The two manifestations may be connected by a distinct lymphangitis, over the course of which during the illness there may crop up occasionally numerous blisters, pustules, or smaller boils.

Sometimes the lesions remain limited to the skin. These cases are distinguished as a particular form of plague under the name of *cutaneous plague* or *pustular* plague. The general symptoms are the same as those of glandular plague, but are mostly of a milder type, and the termination, apart from the local destruction, is often favourable (Sticker). Occasionally the carbuncles have an abortive course, drying up without further local or general symptoms having set in (Pruner).

Secondary plague boils only come under observation during the course of the development of the buboes. They form over or near to the buboes, and are apt to be multiple. They are often very numerous, and are apt to recur again and again (German Commission).

In more severe cases a *hæmorrhagic diathesis* may develop, a condition which may be attributed to the effect of the plague toxin.

The hæmorrhages appear on the neck, breast or extremities, partly as punctiform, partly as linear stripe-like lesions, but occasionally they are much larger, and of a red, black, or lead coloured hue ; occasionally they are so numerous that almost the entire skin is covered by them. Hæmorrhages may also occur from the nose, mouth, lungs, stomach, intestine, kidneys and female genitals ; women in consequence often miscarry. The hæmorrhages usually appear at the height of the illness, from the third to the seventh or eighth day, but sometimes they set in during the first stage. Some epidemics are distinguished by the frequency of such hæmorrhages, whereas, as in the last epidemics in Hong Kong and Bombay, they were rarely seen.

The following are stated by the German Commission to be additional signs and symptoms of infection : extreme feebleness of the heart, with complete paralysis of the peripheral arteries ; severe symptoms of irritation of the stomach and intestine with uncontrollable vomiting and diarrhœa, and evacuation of clots of blood. At the same time there is almost always great tenderness in the stomach and iliac regions and pains in the loins. At autopsies considerable hyperæmia and an ecchymosed condition of these organs are found.

During the later stages of the disease secondary *pyæmic* conditions, such as abscesses, gangrenous erysipelas, parotitis and inflammation of the thoracic glands, changing to suppuration and gangrenous disintegration sometimes develop (Jablonowski).

The German Commission observed quite early, often on the second but even on the first day of the disease, occasional parenchymatous *inflammation of the cornea*, which attacked both eyes more frequently than one. The result was frequently irido-cyclitis, with complete destruction of the eyes due to suppuration ; this concomitant is probably also due to secondary infection.

Death may take place in any stage of the disease, but most frequently occurs on or about the third or fifth day. Sometimes it occurs quite suddenly in consequence of cardiac paralysis, but is sometimes heralded by a very frequent, small, soft, hardly perceptible and often irregular pulse, coldness of peripheral parts with internal heat, occasional cyanosis or lividity of the face, hiccough, and subsultus tendinum. In other cases death is caused by suffocation in consequence of extensive inflammation of the cervical region ; by severe hæmorrhage from the lungs ; from the large femoral veins being laid open by suppuration and gangrene ; from meningitis, septicæmia, or even marasmus.

When plague has a favourable termination a gradual decline of the virulence of each symptom takes place and the *convalescent stage* is reached. Convalescence usually sets in at a period varying from the end of the first to the fourth week. It is generally of long duration, and sequelæ often develop (see below), so that usually one to four weeks elapse before recovery. During convalescence the decrease of the vitality of the tissues is remarkable, incised wounds often remaining unchanged for days. Buboes which have suppurated take from one to three months to heal. The rapid course of pulmonary tuberculosis in plague convalescents, who before having plague only suffered with slight chronic pulmonary disease, shows a considerable disturbance of vital power (Sticker).

2. Septicæmic Plague, Plague Sepsis, or Blood-plague.

(The PESTIS SIDERANS of older observers.)

This variety of plague, owing to the presence of the bacillus in the blood, partakes of the nature of a general infection rather than of a local bubonic character. In addition to buboes, which are frequently accompanied by secondary glandular enlargements in other parts of the body, a seemingly slight bronchial catarrh may develop ; and in a few cases symptoms of general sepsis appear, without a primary lesion on any part of the body having been visible during life. These cases, according to the experience of the German Commission, are characterised by high fever, with a very frequent, weak pulse ; delirium, or immediate collapse ; a rapidly developing sensitive splenic enlargement ; some tenderness of many lymphatic glands (or all those accessible for examination) without distinct enlargement ; stomachic and intestinal hæmorrhages. The presence of the plague bacillus in the blood is generally only confirmed a few hours, or more rarely, a day or two, previous to death, and is sufficient to indicate an early fatal termination. This, as a rule, takes place on the second or third day, sometimes even within the first twenty-four hours.

3. Pneumonic Plague, or Pulmonary Plague.

Childe first called attention to this form of plague. It is ushered in by a chill, followed by increase of temperature, headache, dizziness and pains in the limbs, accompanied by the signs and symptoms of a severe attack of pneumonia, viz., pain and a sensation of tightness in the chest, with cough and expectoration ; deep and accelerated respiration—sixty or seventy per minute, cyanosis, diminished resonance over one or more lobes of the lung and rhonchi. The fever is high, remittent or irregular (see fig. 5, p. 16), the pulse is frequent and weak. There is complete prostration, sensitiveness of peripheral lymphatic glands, and a splenic enlargement, often of considerable size. That, however, which is of great importance for a differential diagnosis is the fact that, as happens in the other forms of plague, herpes never appears (Childe). The expectoration, in typical cases, consists of a sanguineous fluid, which is sometimes expectorated in enormous quantities, and in which multitudes of plague bacilli are found, either in pure culture or mixed with other bacteria, such as diplococcus pneumoniæ, streptococci, or the bacilli of influenza (see fig. 6, plate I.). Rust-coloured sputum, as in ordinary pneumonia, is rare. Frequently, also, cough and expectoration are completely absent (Russian Commission). In most cases pneumonic plague has a fatal termination, which as a rule takes place on the third or fourth day through œdema of the lungs.

Sometimes the illness has a course similar to that of simple bronchitis, without pronounced general and local symptoms, and death occurs quite unexpectedly (Hossack.)

Pneumonic plague occurs much more frequently than is generally supposed, often escaping recognition. Persons suffering with chronic pulmonary diseases, especially phthisis, are particularly susceptible, the plague bacillus seemingly finding a favourable soil for its settlement in tuberculous centres. In plague epidemics, therefore, the mortality of consumptives rises to an alarming extent with the plague mortality. This was particularly observed in Bombay.

Though hæmorrhages from the lung of a severe nature were not noted in Bombay, pneumonic plague doubtless explains those cases of the disease which have been described as occurring in some former epidemics in which hæmorrhage was a prominent feature. In some of these epidemics, as for instance those in Gujerat and Ahmadabad (India) in 1820, and in Pali in 1836, hæmorrhage was so pronounced, and impressed the epidemics with so peculiar a stamp, that the opinion at the time was that though the disease was one very similar to bubonic plague, yet specifically it was a different illness ; therefore besides Oriental Plague, *Indian* or *Pali Plague* was differentiated. This form of disease does not seem to have occurred in the more recent epidemics. In the Hong Kong epidemic of 1894 pneumonic plague was not observed, or was perhaps not recognised.

Secondary pneumonia, which sometimes sets in during the course of bubonic plague, is to be differentiated from primary pneumonia. The secondary variety is set up either through metastatic embolical processes, or through the aspiration of plague bacilli, when the mouth or pharyngeal cavity form the primary seat of the disease ; on the other hand, it may be the consequence of a secondary infection.

4. Intestinal Plague.

A form of the disease which Wilm observed in Hong Kong in 1896 may be designated intestinal plague. It runs its course without buboes, and its predominating features are disorders of the intestinal canal, vomiting and diarrhœa with the evacuation of blood and mucus, so that the entire illness can be classed as an intestinal ailment; *post-mortem* examination demonstrates the fact that the intestinal mucous membrane is the seat of pathological change. Such cases never came under observation during the first epidemic of plague in Hong Kong (1894), nor were they observed in Bombay.

5. Pestis Minor and Abortive Ambulatory Plague.

Mild cases of plague, which occasionally are observed to precede or follow plague epidemics in infected countries for months or even years, are designated *pestis minor*. The disease may be acute, or may run a more chronic course, during which, without any symptoms of serious indisposition, without even fever, buboes usually of the inguinal glands develop, and these may suppurate or become absorbed. It is stated that the epidemic in Mesopotamia during 1876-1877 was preceded for two or three months by afebrile glandular swellings, which continued for two months after. Several years before the outbreak of plague on the south coast of China idiopathic buboes prevailed there. Epidemics of the kind have, however, been observed without being accompanied by plague ; and, on the other hand, actual plague also occurs without preceding or subsequent pestis minor. An illness designated " glandular sickness " occurred in the town of Astrachan in 1877 ; more than 200 cases came under observation, they all had a favourable course, and no development of a plague epidemic came about (Simpson). Pestis minor appeared in Singapore and the Straits Settlements at the same time as it did on the coast of China ; actual plague, however, only broke out there in 1899. Pestis minor was observed in Calcutta during 1895 and 1896; actual plague, however, only appeared there in 1898.

There are no reports as to the incidence of pestis minor in Bombay.

Cunningham found bacilli in the blood in cases of pestis minor in Calcutta ; they were, however, non-infective, and did not seem identical with true plague bacilli, which it is to be noted are only found in the blood in the latest stages of plague. Pestis minor, moreover, is not distinctly contagious, nor during its prevalence has disease amongst rats been observed. From these grounds it seems to me questionable if the cases of illness which have hitherto been called pestis minor have anything at all to do with plague, or if they are not more likely identical with *climatic buboes* which symptomatically resemble them. This question can only be answered by bacteriological examination (see diagnosis).

Many mild disorders with indefinite symptoms which occur during an epidemic appertain, on the other hand, to plague. Such are pains in separate groups of glands, depression, dizziness, headache, slight digestive ailments, short attacks of fever, unusual perspirations, pains in the limbs, &c. That these are really *abortive* cases of plague is proved by the facts that the patients reside in houses, or belong to families that at the time were severely visited by plague, that the disorder leaves behind a weakness or great excitability of the heart which often persists a long time, and, as seen by the German Commission in two cases, the patients sometimes are

liable to the sequelæ to be mentioned below.   Occasionally, also, these
ambulatory cases may have a fatal issue quite suddenly and unexpectedly.

The *mortality* in plague is always very high.   According to Lowson
the mortality in Hong Kong, in 1894, of persons affected with the disease
was as follows : of 2,619 Chinese, 93·4 per cent. died ; of 11 Europeans,
18·2 per cent. ; of 10 Japanese, 60 per cent. ; of 13 Indians, 7·7 per cent.
In 1896, according to Wilm, the mortality in Hong Kong averaged 85 per
cent. ; in Formosa, according to Ogato, 56·1 per cent. ; and in Bombay,
according to Yersin, in 1896-1897, 50 per cent. of the Europeans and
85 per cent. of the natives who were attacked, died.

The following *sequelæ* are to be noted : glandular suppuration of
long duration, arthritis (particularly of the knee-joint), suppuration, otitis,
gangrene of the lung, tedious hæmorrhages from the urethra, dropsy, long-
continued paralysis of the controlling influence of the vagus on the heart,
vascular paralysis continuing for weeks, aphonia and aphasia, jaundice,
deafness, dumbness, paralyses of different kinds (of the face, eye-muscles,
palate and larynx : also hemiplegia and paraplegia), ataxia, and aberra-
tions of mind.   The German Commission is of opinion that the above-
mentioned disturbances of the nervous system are in all probability
intoxications.

PATHOLOGICAL ANATOMY.

Plague cadavers frequently exhibit no emaciation.   Rigor mortis
is mostly pronounced.

The most marked, constant, and characteristic pathological changes
in plague are met with in the lymphatic system.   All the lymphatic glands
of the body are more or less affected.   Even in cases, such as pneumonic
plague, in which there is no primary bubo, enlargement of separate groups
of glands occurs.   It will thus be noted that there is no form of plague
without glandular affections, even when these are not always perceptible
during life on account of their deep situation, or in consequence of their
small size, softness or painlessness, or the corpulency of the patient.
Besides the glands the lymphatic apparatus of the various organs parti-
cipate in the affection.   According to Aoyoma, the mesenteric glands and
the follicles of the intestine are found enlarged, even when the sub-
maxillary, cervical, or axillary buboes are the prominent lesions.   Further-
more, swelling of the tonsils, of the fungiform papillæ of the tongue, and
occasionally of the follicles of the mouth, pharynx, and the cardiac end
of the stomach are present.

The *primary bubo*, which indicates the point of entrance of the plague
virus, is distinguished by its marked *hæmorrhagic* character from the
secondary glandular swellings caused by infection by way of the blood-
vessels.   The periglandular tissue is infiltrated by a serous, gelatinous
fluid, and is permeated by more or less extensive hæmorrhage.   This
œdematous hæmorrhagic infiltration, by means of which the borders of
the separate glands are frequently entirely obliterated, may extend still
further to the adjacent adipose tissue, fascia, muscles, vascular and nerve
sheaths.   The veins adjacent to the buboes occasionally exhibit infiltrated
walls and hæmorrhages into the intima, affording the plague bacilli a
means of entrance into the blood (Bitter).   The glands on section appear
of a dark red colour, which is either diffused over the whole of the cut
surface, or it occurs merely as dark specks dotted over the surface.   The
tissue of the gland is often so soft and pulpy that it breaks down and runs

away on incision. As a rule no difference is perceptible between the cortex and the interior, and no prominence of follicles can be distinguished. The lymphatic vessels in the vicinity of the hilus are usually found considerably enlarged.

The *microscopical* examination exhibits acute inflammation with extravasation of blood. The tissue is infiltrated with red blood corpuscles, leucocytes, and bacilli. According to Yamagiwa the process commences in the capsule, the periglandular tissue, and the subcapsular lymph sinuses. The walls of the veins are infiltrated and relaxed—a fact that explains the occurrence of the hæmorrhages.

If suppuration of the buboes occurs, either a simple abscess formation is found, as in bubo from soft chancres, or a necrosis of the gland substance has taken place.

The characteristic changes described may be limited to a single gland, which then represent the primary seat of disease.

In other cases the primary bubo extends considerably, superficial buboes frequently binding with the deep glands of the abdomen and thorax. Thus the inguinal buboes may proceed by way of the femoral ring to the sacral and lumbar glands and along the spinal column to the diaphragm, while the cervical and axillary buboes proceed towards the mediastina. In such extensive buboes the more peripheral glands, according to Sticker, show a milder, and the glands situated nearer the centre of the body a more severe, degree of disease; although the newer stage of the process appertains to the centrally situated glands, and the older stage to those in a peripheral situation.

In *secondary enlargements* of the *lymphatic glands*, the buboes are not usually of so large a size, nor is the hæmorrhagic character so pronounced as in the primary buboes. They exhibit a greyish-red colour on their cut surface, they are not so juicy, and the infiltration in their vicinity is also absent. According to Bitter the bacillary contents are very different; generally in the primary bubo enormous numbers of bacilli are met with, but no more are found in the secondary glandular hyperplasia than in the blood and spleen, and sometimes there are even far fewer.

The *general tendency to hæmorrhage* is a further pathological characteristic of plague. This tendency is exhibited in numerous hæmorrhages in the most diverse interior organs, such as the stomach, intestine, kidneys, urinary passages, on the serous membranes, &c. They are most pronounced, however, in the septicæmic form. Hæmorrhages into the cutaneous tissues also occur, though not so frequently as those in the organs; and in some epidemics especially they are so numerous that the whole body appears black, hence the designation of *Black Death*.

As to the remaining pathological appearances, the *brain* and *cerebral meninges* are usually congested, and occasionally exhibit hæmorrhages. Sometimes a serous, or sero-suppurative, exudation is found in the recticulæ of the pia mater, particularly along the vessels; and the quantity of fluid in the cerebral ventricles is increased; both contain numerous bacilli.

The *spinal meninges* exhibit the same changes as the cerebral meninges.

Ecchymoses occur on the *pleura*, but exudations are seldom met with in the pleural cavity; in primary buboes of axillary glands pleural changes occasionally occur on the affected side.

The *lungs* as a rule are œdematous and deeply congested, especially in the lower lobes; hypostasis, hæmorrhages, and hæmorrhagic infarcts are sometimes found. It is very rarely indeed that the bronchial glands

or the glands in the thoracic cavity are affected in plague. With cervical buboes œdema of the glottis is sometimes observed.

In *pneumonic plague* the appearance is that of a typical confluent lobular pneumonia. Areas varying in size from that of a bean to an egg, with blackish-red hæmorrhagic patches, and œdema in their vicinity, are found mostly unevenly distributed over both lungs, especially the lower lobes. When on the surface of the lung these areas exhibit recent pleurisy on their serous aspects. A sticky, stringy juice exudes from the incised surface of these lung patches. In mixed infection lobular hepatisation is also found in different stages. In two cases observed by Sticker the croupous foci exhibited so severe a necrosis and hæmorrhagic infiltration that the lung tissue was on the point of breaking down, which, had it taken place, would have caused serious hæmoptysis, explaining a condition that has been observed in several epidemics. The bronchial tubes contain a frothy, sero-sanguineous fluid, and the mucous membrane of the respiratory tract is reddened. Under the microscope the alveoli of the lungs in the pneumonic areas are found to be almost exclusively filled with blood and bacilli; a few leucocytes and fibrine may be present. The septa of the alveoli become involved and readily break down. The bronchial glands, as also the other groups of glands, may be either enlarged or normal. The foci in the lungs form the primary seat of disease.

The *heart*, especially the right ventricle, is mostly dilated. Petechiæ or ecchymoses are often found beneath the visceral layer of the serous pericardium. The myocardium is frequently seen to be pale, the parenchyma clouded, or undergoing fatty degeneration.

The *liver* is generally enlarged and intensely hyperæmic. Large hæmorrhages are very occasionally seen beneath the capsule. The liver substance itself is generally pale and soft in consequence of parenchymatous degeneration.

In the lungs, and also in the spleen, the kidneys and the muscles, necrosed patches forming abscess-like foci, varying in size from a mere speck to a hazel-nut, and surrounded by a hæmorrhagic area, are sometimes met with. These foci are especially rich in bacilli (Austrian Commission). The bile is copious, of varying consistency, and the wall of the gall bladder is sometimes œdematous. Cholecystitis and pericholecystitis have been met with.

The *spleen*, as a rule, is enlarged, often to a considerable extent ; it is also hyperæmic and soft, and at times almost deliquescent. Occasionally there are hæmorrhages immediately beneath the capsule.

In pneumonic plague Bitter states that the spleen is but seldom increased in size.

The mucous membranes of the *stomach* and *intestine* frequently exhibit petechiæ and ecchymoses, and occasionally also hæmorrhagic erosions are found in the stomach. Aoyama saw follicular hyperplasia in the stomach in a few cases. The solitary follicles and Peyer's patches of the intestine are frequently swollen. Wilm often observed small ulcers with undermined edges, yet without an eschar, in the intestine.

Wilm found the *mesenteric* glands to be frequently, but only slightly, swollen.

The retro-peritoneal glands, when involved, become of a dark bluish-red colour, and are frequently met with in the softening stage surrounded by extravasations of blood.

The blood-vessels and lymphatics between the affected glands and the intestine are seen to be mostly dilated and of a reddish or reddish-blue

colour ; extensive hæmorrhages occur also between the layers of the mesentery.

The *kidneys* are often enlarged and congested, the cortical substance thickened, and the parenchyma in a state of cloudy or fatty degeneration. The surface of the kidney capsule, the mucous membrane of the pelvis of the kidney, and the peri-nephric tissues are frequently the seat of more or less extensive hæmorrhages.

The pelves of the kidneys are sometimes occupied by coagulated blood, proceeding even into the ureter.

The *urinary bladder* is sometimes filled with bloody urine, and its mucous membrane ecchymosed.

Sticker found the *bone marrow* in a condition of swelling and hyperæmia.

DIAGNOSIS.

The diagnosis of plague is difficult, particularly at the commencement of epidemics. In severe cases it has to be differentiated from malignant cases of *malaria, typhus*, and perhaps also from *recurrent fever*. Mild cases may be taken for *venereal buboes* and other *inflammations of lymphatic glands*. Skin lesions in plague may be mistaken for *anthrax*, and pneumonic plague for *croupous pneumonia*.

The epidemic character of the disease, the severe general symptoms ushered in with high fever, and the presence of buboes serve to characterise the disease. Even though the latter may not be present in septicæmic cases the presence of buboes in other cases allow no doubt as to the diagnosis. It may be necessary to distinguish dengue fever from plague; in dengue we find slight enlargements of the inguinal, axillary and cervical glands, but the severe pains in the joints and muscles, the peculiar exanthema, and the benign character of the ailment are sufficient to differentiate between the diseases.

In doubtful cases, more especially those in which no buboes develop, *bacteriological examination* is of primary importance. Besides fluid from buboes, the sputum (in the pneumonic form), the blood (in the septicæmic form), urine (taken under aseptic precautions), the contents of pustules and boils, may all be used for examination. Should the microscopical examination not confirm the diagnosis, cultures should be made, either on agar-agar or in bouillon, and then experiments on animals, conducted with these cultures. The Austrian Commission recommend guinea-pigs as the most suitable for this purpose.

The *serum diagnosis* is of less practical importance. True, the serum of plague patients generally reacts specifically (agglutinating effect) on a solution of pure culture of plague bacilli, in the same way as typhoid serum on typhoid bacilli and cholera serum on cholera bacilli; this reaction, however, is, on the one hand, never extant during the primary stage of the disease when it would be of particular importance, and on the other hand is not present in all cases.

Zabolotny's experience was that serum of plague patients did not agglutinate at all during the first week, it agglutinated slightly during the second week, and during the third and fourth weeks (convalescence) it agglutinated powerfully. Moreover, according to Sticker, the agglutinating effect of the serum only appears distinctly after very severe cases of illness, and the severer the illness the more distinct the reaction ; it fails entirely in abortive cases, and is even occasionally lacking in conva-

lescents from severe attacks (German Commission). The serum diagnosis can therefore not be applied for the elucidation of the open question as to the relation of pestis minor to actual plague ; this can only be decided by the examination of fluid from the bubo, or of an excised lymphatic gland.

PROGNOSIS.

Plague surpasses all other infectious diseases in danger, and is therefore always a very serious illness. The prognosis, in the first place, depends (1) on the *character* of the existing *epidemic*, which may be more or less malignant ; (2) on the period at which the illness sets in, attacks during the later period of an epidemic being as a rule milder than those at the beginning ; (3) on the *age* of the person attacked—strong adults are relatively less endangered than children and old people, who nearly always succumb ; (4) on the *position of the primary bubo*, inguinal buboes giving the most favourable, cervical buboes the most unfavourable, prognosis, while axillary buboes take a medium position. The *condition of the heart* is of great importance ; a full and regular pulse is a good sign, a weak and irregular pulse is correspondingly bad.

Multiple buboes, obstinate vomiting, the early appearance of diarrhœa, cerebral symptoms, anæmia, hæmorrhages, the presence of bacilli in the blood—all these are unfavourable prognoses, and, almost without exception, indicate approaching death. Should the patient survive the sixth day a favourable termination may be hoped for, as according to Wilm, 70 per cent. of all patients succumb within the first six days. Suppuration of the buboes is not in itself a favourable sign, except in so far as suppuration usually only occurs in the second week, so that the patient must by then have already survived the most critical time.

PROPHYLAXIS.

The correct diagnosis of the first cases of plague is, as in cholera, of the greatest importance. If these are recognised it is quite possible to nip the epidemic in the bud, or at least to confine it to a small centre. This result is more likely to be obtained in plague than in cholera, as plague at the commencement of its appearance amongst a community spreads more slowly than does cholera. It is therefore the duty of the respective States, on the appearance of suspicious cases of disease, to at once send competent experts to the place to confirm the nature of the illness and also to insist upon the declaration of all suspicious cases of illness.

The measures to undertake after the outbreak of plague are as follows : *Isolation of the patients and disinfection of their excretions ; the removal of all persons, even the healthy, from plague-stricken dwellings, and the observation of all who have been in contact with the patient. The disinfection of the house together with the effects of the inmates ;* the destruction and subsequent burning of the *rats* and *mice*, and also strict *house to house inspection* for the discovery of concealed cases. The dwellings in the vicinity of the plague-stricken houses must be treated in the same manner as those found to be infected.

Besides steam sterilisation and dry heat up to 100°, the following *means of disinfection* appear, from experimental research, to be the most suitable : corrosive sublimate 1 per cent., to which Haukin advises the addition of hydrochloric acid in the proportion of 2 in 1000 ; sulphocarbolate 1 per cent., chlorinated lime and quick lime, although

weaker, are also to be recommended on account of the simplicity of their use and their cheapness.

In *India* the method of removing those suspected of contagion (contacts) to segregation camps is highly to be commended. These segregation camps consist of huts quickly improvised of bamboos and mats and situated in open fields. After ten days, during which time their dwellings are disinfected, the contacts are allowed to return to their homes. Should cases of plague occur in these segregation camps, the huts in question are burned. Sublimate and lime are principally used as disinfectants ; the walls of houses are washed down with a solution of sublimate and are then freshly whitewashed. Moreover, the slates are taken off the roofs to afford entrance to light and air, and should the floor be a mud floor it is dug up to a depth of four inches and disinfected with chlorinated lime.

As Wilm was able to confirm bacilli in the urine,[1] for four to six weeks after the expiry of the first acute stage of the disease, it is necessary that the isolation of the patients in cases of recovery should be maintained for six weeks. It is advisable, also, to provide the patients with mosquito nets, in order to prevent a possible dissemination of the plague by means of insects (mosquitoes, fleas, flies, &c.). In pneumonic plague it is advisable that doctors and attendants should protect themselves from the danger of contagion from the particles of sputum sprayed out from the patient's mouth in coughing, &c., by tying sponges over their mouths and noses, these sponges to be disinfected every time after use. The patient should be covered with a fine-meshed veil. The bodies of persons who have died of plague should be—as soon after death as possible—well coffined, and buried in graves at least three metres deep, or cremated.

Wilm considers that strict superintendence of the water supply is imperative. Articles of food gnawed by rats in times of plague should be destroyed. Perhaps, also, attention should be directed to cattle about to be killed for food, more particularly pigs.

It is of great importance when plague breaks out in a country to have the *first plague centre* entirely *barricaded off* by a military cordon. This is quite possible if the centre be a small one, as, amongst other instances, was evidenced in the little town of Noja in lower Italy in 1815 ; but even a strictly maintained blockade has been rendered illusory through the medium of rats. Once the illness has, however, gained a hold and taken in larger areas of land, which is mostly apt to be the case before plague is recognised and the efforts to establish a diagnosis are overcome, the cordon principle is no longer practicable. Then nothing remains to be done except to *supervise*, as strictly as possible, the lines of communication, the country roads, the railways, the rivers and canals, along which traffic passes. At certain junctions sheds should be erected, in which all travellers coming from plague-stricken districts should be medically examined, and the sick or suspects should be isolated and their linen, clothes, and other belongings disinfected, although it is better to burn the things belonging to the patients. In the plague-stricken towns, departing travellers should be examined at the railway stations and at the docks before embarking.

As long as an epidemic rages, *all arrangements connected with the assembling of crowds*, such as annual fairs, parties, excursions, &c., should be *prohibited*. The pilgrimages to Mecca are a great danger to the Eastern Hemisphere, immense numbers of persons from all the Mohammedan countries assemble here yearly, among whom an outbreak of plague might have most calamitous consequences. Having realised this danger

[1] Gotschlich lately also found virulent bacilli in the sputa of three cases of recovery from pneumonic plague weeks after seemingly complete restoration to health.

several States have, during the latter years, forbidden the pilgrimages to Mecca, or have at least restricted them.

As the importation of plague into other countries can take place by land and water, sanitary police supervision should be established on *the frontiers as well as on ships.* For this purpose, on that quarter from which importation is threatened, as for instance at custom houses, stations for examination, provided with quarantine necessities and disinfecting appliances, should be erected where the sick and suspects are detained and the infected luggage disinfected. The travellers permitted to proceed must be watched during their journey and at their destination until the end of the period of incubation (ten days). Crowds of travellers such as emigrants and pilgrims, whose hygienic conditions are usually unfavourable have to be submitted to a ten days' quarantine.

The sanitary police supervision of the *maritime commerce* has to extend to all ships—sea or river—coming from plague-stricken harbours. Ships which have, or have had, plague patients on board must go into quarantine, and the patients must be isolated in special quarantine hospitals ; it is best to burn the linen and clothes of the patients ; and the luggage of the healthy crew, passengers, &c., as also the ship itself, must be disinfected. Ships on board which no cases of plague have occurred during the voyage are to be exempted from these measures.

The measures resolved on at the *Sanitary Conference* held in Venice in 1897 are of particular interest. Vessels coming from plague regions are distinguished as infected, suspicious and unsuspicious. (1) " Infected " is a vessel on board which plague rages, or on which one or more cases of plague have been confirmed within the last twelve days ; (2) " Suspicious " is a vessel on which, at the time of departure or during the voyage, plague has appeared, but on which, during the last twelve days, no new case has been observed ; and (3) " unsuspicious " is a ship which has had no case of plague on board, either before starting, during the voyage, or at the time of its arrival. In the case of plague-stricken vessels the following procedure must be carried out :— Disembarkation and isolation of the patients, examination of the other persons on board, who have also to be disembarked and isolated for about ten days (according to the sanitary conditions of the vessel and the state of the last case of plague that appeared on board), disinfection of all those parts of the ship in which plague patients have been, and also of the soiled linen, clothes, and other belongings of the infected persons, the baggage of the crew and travellers, if these be considered infective by the port sanitary officer. The bilge water must be pumped out of the ship after previous disinfection, and fresh drinking water supplied after a thorough cleansing of the reservoirs. In suspicious vessels medical examination and supervision of the travellers for ten days is indicated ; this consists in their being allowed free intercourse, but wherever they go they are supervised and subjected to medical examination, while the disembarkation of the crew should be delayed. The same regulations hold good, as far as the crew and travellers, &c., are concerned, for suspicious vessels as for plague-stricken ships. Finally, unsuspicious vessels may, as a rule, be admitted to unrestricted intercourse. As to ships that carry travellers in large numbers (emigrants or pilgrims), particular measures are adopted suitable to each case.

The disinfection of the bilge water of the ship is done with lime so mixed with the water that it becomes a 5 per cent. solution (Abel).

Attention should also be directed on ships to sick and dead *rats*, and as these animals are good swimmers the vessel should not be allowed to approach the quay or wharf. Articles of food, gnawed by rats, must be destroyed.

A supervision of goods-traffic has also to be undertaken, but as goods in general have a relatively small chance of becoming infected no extensive measures likely to seriously affect commerce are necessary. It suffices to exclude from commerce such articles as can be infected by plague patients from a plague-stricken country. The latest German prohibitions are quite adequate, only forbidding the importation from Asia,

Egypt, &c., of body linen, old and worn articles of apparel, second-hand
bedding, and rags of all kinds.

Finally, *improvement of sanitary conditions* play a great part in the
prophylaxis of plague, for, as seen above, the origin and development of
the pestilence is connected with hygienic errors. The latest epidemics,
even, have given striking proofs of this fact. The prophylactic annihila-
tion of rats and mice in places threatened by plague is also of the greatest
importance, and may be accomplished by placing in their runs tow
covered with phosphorus, strychnine on wheat, sulphuric acid, fresh
squills, &c.

Personal prophylaxis consists in a regular manner of living, scrupulous
cleanliness, and care of the skin, as also the avoidance of coming into
contact with the plague-stricken and their dwellings and effects.
Formerly the inunction of the body, and more particularly of the face
and hands with oil was recommended, a measure based on the observation
that oil-carriers, and oil and fat dealers, were seldom affected by plague ;
but experiments have failed to confirm this theory. Valuable experiences
on *protective inoculations* have been gathered, these relating to so-called
active as well as to passive immunisation. Active protective inoculation
was practised by Haffkine, who used bouillon cultures of plague bacilli a
month old, grown at a temperature of 30° C. and killed off by warming
for an hour at 70° C. Yersin used for this purpose the serum of horses
immunised by being inoculated with cultures killed by warming.
Although experimental inoculations on animals with both methods yielded
affirmative results, Haffkine's method only was successful in regard to
human beings, who are much more susceptible to plague than the
experimental animals used, so Yersin's method was given up. Even
though Haffkine's protective method does not afford absolute immunity,
yet numerous statistics published certainly prove that of persons
inoculated relatively fewer fall ill, and of those that do fall ill fewer die
than in the case of the uninoculated. According to Haffkine, the
difference in mortality from plague between the inoculated and the
uninoculated parts of a community was on an average 80 per cent., and
the death-rate as regards inoculated plague cases was 50 per cent. lower
than in the uninoculated. The duration of protection is supposed to be
at least four to six months.

The inoculations as a rule are made on the upper arm or abdomen. The quantity
injected is, for adults $2\frac{1}{2}$ to 3, for children $\frac{1}{2}$ to 1, ccm. Haffkine prefers a second
inoculation ten days after the first, and a third one again ten days later. The draw-
back to these inoculations is that they are accompanied by disagreeable concomitants,
consisting in a more or less pronounced local and general reaction, such as fever,
uneasiness, low spirits, general articular and muscular pains, headache, loss of appetite,
nausea, vomiting, diarrhœa, painful infiltration at the locality of the injection, pains
and enlargement of the corresponding lymphatic glands, symptoms which last several
days.

On the outbreak of an epidemic it would be practically impossible to
inoculate the entire population, so as a rule the inoculation is confined
to the inmates of plague houses, and all those who, in consequence of
their occupation, are particularly exposed to the dangers of contagion,
such as doctors, attendants, persons engaged in handling or burying
corpses, and persons occupied in the cleaning and disinfection of plague
houses.

TREATMENT.

The treatment of plague is symptomatic and Cantlie considers the results by no means so hopeless as is generally supposed. The relatively low mortality observed in Europeans is attributed by this author to early and suitable therapeutics. But in this connection the fact must not be lost sight of that Europeans usually seek advice for slighter illnesses than do the natives. Cantlie at the beginning of the illness recommends alteratives, especially calomel (5-10 grains) which after five hours should be followed by a saline. Stimulants (alcohol, ether, camphor, musk, caffeine, &c.) should be administered early. Lowson praises the inhalation of oxygen.

In Bombay good results were attained by large doses of hydrar. perchlor., for which plague patients exhibit a peculiar tolerance. Syphilitic persons, who are more or less saturated with mercury, overcame the illness better than others, an observation which could be frequently confirmed in prostitutes.[1] Fever requires antipyretic treatment, cold applications to the head, cold spongings, packs, and such antipyretics as quinine, antipyrin, phenacetin, &c. If a tendency to sweat appears, the same should be encouraged by hot drinks. Cantlie found that restlessness and sleeplessness were best relieved by hyoscine (0·006 subcutaneously). For vomiting, mustard poultices over the epigastrium, ice and morphia are used.

The *buboes* and *carbuncles* are treated with fomentations of sublimate and warm poultices ; when there is fluctuation, an incision should be made. Leumann warns against the too early incisions of buboes which have not yet suppurated, as in two such cases death rapidly followed. Injections of carbolic acid, sublimate, or tincture of iodine into the glands have not proved efficacious. Yamagiwa considers the early extirpation of glands rational, as these represent the primary seat of the disease and by this treatment enormous numbers of the original plague-infecting bacilli are removed ; in two cases he saw favourable results follow the operation. On the other hand, a case is communicated in the report of the German Commission in which death from plague-meningitis followed the excision of the buboes.

When *hæmorrhages* set in, styptics, such as tinct. ferri perchlorid., ergotin, &c., should be tried.

In *pneumonic plague*, stimulants and expectorants are indicated. The inhalation of a spray of 1 per cent. carbolised lime solution may also be tried.

The serum therapy which yielded such good results on animals, has not been successful as regards man. The same holds good with the serums of Yersin and Lustig. The latter was taken from animals that had been immunised by a nucleo-proteid gained from cultures of plague on agar-agar. Perhaps in the future it will be possible to prepare a stronger serum which may be efficacious for human beings also.[2]

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[1] *Brit. Med. Journal*, Jan. 1, 1898, p. 46.
[2] The serum recently prepared by Roux is said by Calmette to have a better effect. Of 104 plague patients treated therewith in Oporto, 13 died, whereas the mortality previously averaged 33 per cent. (*Bulletin Méd.*, 1899, No. 85).

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II.

DENGUE FEVER.

DEFINITION.

Dengue Fever is an acute infectious disease, distinguished by the appearance of an initial and terminal polymorphous eruption, and accompanied by severe articular and muscular pains; dengue fever is confined for the most part to warm climates.

SYNONYMS.

Bouquet, *i.e.*, the Piebald ; Knockelkoorks, *i.e.*, Articular fever ; Pantomina, Piadosa, *i.e.*, the Mild ; Colorado, Trancazo, *i.e.*, Stroke ; Polka (because the appearance of dengue fever in Brazil fell simultaneously with the introduction of the polka), Plantaria, Gaditana, Calentura roja, Rosalia, Zamparina, Andancio ; Abu-Robake, *i.e.*, Father of the knee, Knee-ailment ; Bou-Bou, *i.e.*, Fear, Terror, the strength-breaking disease (Arabia) ; *Abu-Dobus* (Benghasi); *N dagamonté, N'rogai* (Senegambia); *Baridiyabis, Hema Mguu, Abu-ndefu, Kindinga Repo, i.e.*, spasmodic pains (Zanzibar) ; *Bonon, i.e.*, sighs (Sandwich Islands) ; *Rheumatismus febrilis exanthematosus, Rheumatismus febrilis epidemicus, Exanthesis arthrosia, Exanthesis rosalia, Scarlatina mitis, Scarlatina rheumatica, Arthrodynia.*

The word *Dengue* is variously explained. According to Zulzer the name originates from the Spanish and is related to the English word "*dandy,*" the illness taking its name from the mincing walk peculiar to those affected. According to Ornstein, dengue is an Indian word expressive of the sensation felt by a sound ringing through the brain, like a violent blow on the drum. According to v. Düring, it can be traced back to ancient Arabic and signifies great depression, languor.

HISTORY.

The history of dengue fever cannot be traced back further than to the last few decades of the eighteenth century. The first reports of the illness were made in 1779, during which year, according to the chronologist Gaberti, cited by Pruner, it reigned in Cairo, and also in Batavia as reported by the town medical officer, Bylon. During this and the following year the illness seems to have had a larger dissemination in tropical and subtropical regions both in the Eastern and Western Hemispheres. In 1780 it was observed in Philadelphia, on the Coromandel coast of India, and in Zanzibar ; in 1784-1788 it was observed in Southern Spain (Cadiz, Seville) ; in 1824 dengue fever appeared in India and Suez ; in 1827 in the Antilles and the Lesser Antilles, in Curaçao, and in New Granada ; in the following year on the Gulf and Atlantic Coast of the Southern States of North America as far north as Philadelphia, in Vera Cruz, and on the Bermuda Islands. A third pandemic which lasted till 1873, originated in Zanzibar in 1870 and spread thence to Aden, the Arabian coasts, Port Said, Burmah, China (Shanghai, Amoy), Formosa, the Malayan Peninsula, India, Cochin-China, Mauritius and Réunion ; and the cases that Wernich saw in Hong Kong in 1876 were probably offshoots of this pandemic. Between these pandemics only isolated, circumscribed outbreaks of the

illness were observed in various countries ; periodically it seems entirely to disappear off the face of the earth. The last extensive epidemic of dengue fever which directly preceded the influenza epidemic, raged in 1889; Egypt, Palestine, Syria, a large part of Asia Minor, Greece, Turkey, Cyprus, Rhodes, and the Islands of the Archipelago being visited by the disease.

GEOGRAPHICAL DISTRIBUTION.

In EUROPE dengue fever has hitherto been observed in Southern Spain, Greece, Turkey, on the islands of the Grecian Archipelago, Crete, Rhodes, and Cyprus ; in ASIA : in Asia Minor, Syria, Palestine, the coast of Arabia, in India, Thibet, Burmah, Cochin China, China (Hong Kong, Amoy, Shanghai), in Formosa, in Manila, and in the Malayan Archipelago (Java, Sumatra, Celebes); in AFRICA : in Egypt, Tripoli (Benghasi), Senegambia, on the East Coast, on the Canary Islands, Réunion and Mauritius ; in AMERICA : in the Southern States of the United States, in the Bermudas, in Mexico (Vera Cruz), Honduras, the West Indies, in Curaçao, on the northern coast of South America, in New Granada, Peru (Lima, Callao) and Brazil ; finally in Tahita and the Sandwich Islands.

It will be therefore seen that *warm countries* are particularly visited by this illness. In a northerly direction the disease on the Eastern Hemisphere has penetrated to 41° (Constantinople), and on the Western Hemisphere to 40° (Philadelphia), while in a southerly direction it has hitherto not extended beyond the tropics.

In certain countries of its tropical and sub-tropical region of distribution, dengue fever is *endemic*. Thus, according to Sandwith, the illness in Egypt is of annual occurrence during the damp autumn months until December. The illness also often rages in Arabia, Senegambia, Honduras, on the Bermudas, Tahiti, and the Sandwich Islands. We do not know if these districts or any one of them should be regarded as the birthplace of dengue fever, and is thence periodically carried into other countries. According to Zülzer, at least in regard to the more important epidemics, the point of departure of the disorder is generally the islands of Central America, particularly the lesser Antilles in the Western Hemisphere, and the littoral of the Red Sea in the Eastern Hemisphere. Besides these two, de Brun asserts that there is a third centre on the west coast of Africa, in Senegambia.

ETIOLOGY.

Dengue fever is originated by a specific, but hitherto undiscovered, virus of disease. This is, however, probably similar in its nature to the virus of acute exanthema, to which dengue fever is closely allied.

Hunt (according to Hare) found very mobile granules in the fresh blood of patients, as also similar formations in bouillon into which the breath of a patient had been conducted ; Kartulis and other investigators were unable to confirm any microorganisms in the blood of their patients.

Opinions as to the contagious nature of the disease are divided. Whereas formerly it was mostly considered to be non-infectious, at the present time, and especially after the experience of the last epidemics, the conviction as to its contagious character has gained more ground. It has been frequently observed that the arrival of persons suffering with dengue fever, in localities hitherto healthy, has been immediately followed by the outbreak of epidemics, as in ports after the arrival of ships with sufferers

on board, and in the interior after the arrival of troops from infected garrisons. In many instances it was easy to trace how epidemics occurred in the immediate vicinity of the first case of illness, and how from that point further foci developed and the illness progressed through families, houses, streets, &c. That dengue fever is contagious seems to be proved by the frequency with which doctors and nurses are attacked by it, and on the other hand this idea is negatived by the extraordinary rapidity with which the dengue epidemics are wont to spread. In this connection it is, however, to be considered that the incubation period of dengue fever is a very short one; that patients, even from the commencement of the illness, are capable of infecting others; and that once the illness has been imported, the virus of the disease can develop outside the human organism, clinging to the soil or elsewhere and multiplying. In these particulars dengue fever resembles influenza, and, in fact, exhibits so great a similarity to influenza that some few authors have even gone so far as to assert that the two are modified forms of the same primary disease (Hansen), or even declare them to be identical (Cantlie, Felkin). Influenza, also, which formerly was reckoned to be non-contagious is, according to the experience of the pandemic of 1889-1890, now held by most observers to be infectious.

The virus of dengue is readily diffused, so that a casual exposure suffices for the transmission of the illness. Perhaps even the virus may be contained in the breath of the patients.

The *period of incubation* has a maximum duration of not more than four or five days, but it usually lasts one or two days only, often only a few hours.

The virus of the illness can be *carried by means of human intercourse.* By sea it follows the maritime commerce, and in the interior the principal streets, railways and rivers.

In this respect the Indian epidemic of 1871 to 1872 is very instructive. In the course of 1870, as mentioned above, an epidemic of dengue fever broke out in Zanzibar. During the following year the illness was carried to Aden in ships, and at this time the ship "Dalhousie" left Aden, bound for Bombay. On the way some cases of dengue occurred on board, and immediately after the arrival of the ship at Bombay the illness broke out there. In a short time it spread from thence in a southerly direction through the district of Poona and, always following the railway line, broke out in Madras in February, 1872. From Madras the illness was carried by troops to Trichinopoli. Simultaneously, also it spread from Bombay in a northerly direction, always following the railway, and reached Allahabad, Benares, Danapoor and Calcutta. From Calcutta by way of the Hoogli it spread to Barrackpore, Tschandarnagar, and Dacia. A steamer brought it from Calcutta to Rangoon (Burmah). From Calcutta it could, furthermore, be traced step by step to Cawnpore, Fayzabad, Lucknow, Agra, Delhi, Umbala, and to the foot of the Himalayas (to 32° north latitude) (Stuart according to Roux).

Probably the virus of the illness can also be *carried by inanimate objects.*

It is supposed that in 1889 dengue fever was carried to Smyrna through *rags*, which are every year imported for sale from Palestine, Syria and Cyprus, by Jewish rag merchants (Floras).

A *certain high temperature* is necessary for the inception and spread of an epidemic. The summer and the commencement of autumn are the real dengue seasons, especially in those districts that are not actually tropical; the illness almost regularly appears in July and August, rarely in September and then only when the temperature is unusually high. In the tropics also the epidemics mostly occur in the warmest months, or at least only then attain their height; still, epidemics sometimes prevail

when the temperature is relatively cooler, as for instance was proved by the epidemic of 1827-1828 in the West Indies. A great fall of temperature and the appearance of absolutely cold weather always puts an end to the epidemics (Hirsch).

The *moisture of the atmosphere* exercises no influence on the appearance of the illness. Epidemics have come under observation during rainy, as well as during long spells of dry weather. Winds also have no significance, but Corre ascribes *earthquakes* as exercising an influence on the illness.

The *physical and geological nature of the soil* play no part in the development or spread of the disorder. As in yellow fever, *coastal regions* and *towns* are most affected ; the illness is especially liable to appear in those parts of the town which are overcrowded and unfavourably situated as regards hygiene. *Places at high altitude*, consequently cooler, escape for the most part ; still in 1889 villages at an elevation of 1200-1500 mètres on Lebanon were visited by the illness (de Brun).

Immediately the importation of the illness has taken place, the spread of the epidemic, as mentioned above, is apt to follow rapidly. The duration of the epidemic is generally several months, and on the conclusion of the epidemic sporadic cases often occur weeks, months, or even years after ; sometimes dengue fever takes permanent possession of places once visited by the illness, a fact observed by de Brun in Egypt and Syria.

On ships also, epidemics frequently come under observation, especially on such as have come from infected ports ; sometimes, however, without an infection being traceable.

Thus in 1870, dengue fever broke out on board a French man-of-war cruising on the West Coast of Africa in 0·21° south latitude and 2·24° west longitude, without it having been possible that it could have been carried from land or from another ship (Fougue).

The *pre-disposition* to dengue fever is a general one. When a district is visited by the illness, a large part of the population is apt to fall ill. It is not a rare occurrence for two-thirds, three-quarters, or even a larger proportion to be attacked, occasionally only a few escaping.

Neither sex nor age affords immunity ; children only a few days old, and the most aged persons are attacked. The illness has even been observed in newly born infants.

Difference of *race* also plays no essential part. True, in a few epidemics (Antilles, Java, Benghasi, &c.) the observation was made that the negroes possessed a certain immunity ; in others (India, China) that fewer Europeans than natives were attacked ; still in these instances peculiarities of race come less under consideration than other circumstances (possibility of exposure to infection, &c.).

Position and *occupation* have no influence. No immunity is afforded by a previous attack of the illness. Dengue fever not only attacks persons who have had the illness the year before, but even attacks the same individual again and again during the same epidemic. Some persons seem to be particularly predisposed to dengue, being attacked once or several times in every epidemic.

Dengue fever is said also to occur in animals (cows, horses, dogs and cats) in India ; and in America whole herds of cattle are attacked by the disease.

SYMPTOMATOLOGY.

The outbreak of the actual illness is occasionally preceded by *prodromal symptoms* for a couple of days. These consist of general indisposition, depression, giddiness, frequent yawning, gastric disorders, &c.

Generally, however, the *onset of the illness* is markedly *sudden*, often coming as a shock, and occurring mostly at night or in the early morning on rising. Fever sets in accompanied frequently by slight rigors, rarely by shivering fits, these symptoms are rapidly followed by feelings of serious indisposition, pains in the head, joints and muscles, and a rash on the skin spreading over a larger or smaller portion of the body.

The *temperature* rises rapidly and in a few hours reaches its maximum, which according to de Brun is generally 39° to 40°, and is seldom exceeded. Exceptionally, however, temperatures of 42° and even higher have been observed. The fever is generally remittent, seldom intermittent. The *pulse* is accelerated, its frequency averaging 100 to 120; often, however, there are only 80 to 100 beats per minute.

The *headaches* are severe and are usually situated in the forehead, especially the supra-orbital region and in the depths of the orbital cavity.

As to the *joints*, usually the smaller are affected first, later on the larger ones; several are often simultaneously affected, sometimes only single joints. The pains are frequently of an evanescent nature, changing their position. The pain that is characteristic of dengue fever has its seat in the *knee joints;* the pains are increased by walking and occasionally a singular mincing gait peculiar to the illness obtains, and which has caused the introduction of its name of *dandy fever*. According to de Brun the knee joints are not painful on pressure but the muscles crossing them ache on being touched. Occasionally such joints as have been affected before (by injuries, dislocations, arthritis, &c.), are particularly seriously affected. In severe cases the pains are so violent that a light pressure cannot be borne, and the patient is quite unable to make the slighest movement with the extremity attacked.

Occasionally the pains set in with such suddeness, that a movement commenced can scarcely be completed without the severest pains. In some cases the painful joints become reddened, swollen, and hot. Often also, there is œdema of the hands and feet.

The muscular pains have their seat in the loins in particular. Occasionally, also, the muscles of the eyes are affected, so that every movement of the eyelids and eyeballs is painful and restricted. Occasionally isolated tendons exhibit a painful swelling.

Furthermore, sharp, cutting *pains* in the *bones* occur which cause a sensation as if they were being broken, hence the designation *break-bone* fever.

The eruption which appears soon after the commencement of the illness (*initial exanthema*) is as a rule nothing more than a vaso-motor reddening of the skin and is most pronounced on the face, where it may assume a spotty character. The face and eyelids, in addition, are frequently swollen, the skin dry. Isolated parts of the body often exhibit hyperæsthesia, while in other cases a more or less extensive anæsthesia is present.

The following are further symptoms which appear at the worst stage of the illness: the eyes water and are photophobic, the conjunctivæ are

injected, the nose stopped up and its secretions increased; the tongue is thickly coated in the middle, and red at the tip and edges; the breath is foetid, the pharyngeal mucous membrane reddened and inflamed, the tonsils swollen, in consequence of which the patients complain of pain in the throat and difficulty in swallowing. Occasionally the salivary glands are swollen and there is salivation. Occasionally, slight laryngo-trachitis or bronchitis is present, and it is not uncommon for the patients to suffer with severe precordial agony. The appetite as a rule is very bad, on the other hand thirst is increased; the action of the bowels is either constipated or very relaxed. In some epidemics, nausea and vomiting particularly at the commencement of the illness are frequent symptoms. Occasionally enlargement of the liver and slight jaundice are observed (de Brun). The spleen is not enlarged. The urine is diminished, the specific gravity increased, the reaction is acid, and later on may be neutral or even alkaline. Albuminuria seems of rare occurrence.

The patients are uneasy, sleep badly, and are tortured by distressing dreams. Frequently the memory is enfeebled, so that the patients seek in vain for certain names and words, confuse facts, and cannot write down short sentences clearly (Slaughter). Delirium, maniacal attacks, and suicidal ideas occur. In the case of little children convulsions are sometimes observed, and nervous women may have attacks of hysteria. A few cases have been observed in children in which they were comatose for days.

Seven patients of Vernani saw everything of a yellowish-red colour, as if illuminated by a great fire; the ophthalmic condition was negative.

There is, moreover, considerable prostration, and the sufferers become rapidly emaciated and anæmic.

The first stage of the illness generally lasts three days. The eruption is very evanescent, sometimes only existing for an hour, mostly for five or six hours, seldom for longer than a day. The articular pains diminish in intensity, but usually last until convalescence sets in. The fall of temperature rapidly takes place in a few hours, frequently accompanied by profuse perspiration of a peculiar odour. The latter is so strong that it is possible thereby to diagnose the illness from some distance (Slaughter), and is variously described, by some as being sour, by some as resembling rotten straw, or being similar to rue (*ruta graveolens*). It is but rarely that the temperature falls suddenly, so that the normal is only reached after several days. The frequency of the pulse occasionally diminishes to 60 or 70 beats per minute.

Immediately after the apyrexia has set in, or a few days subsequently, mostly between the third and fifth days of illness, a second eruption (*terminal exanthema*) breaks out, sometimes without fever, sometimes accompanied by a renewed rise of temperature, usually lasting only a few hours. This eruption may vary considerably, resembling that of measles, scarlet fever, or urticaria, or it may appear as lichen, roseola, or in the form of vesicles, blisters or pustules. The face, hands, forearms and chest form its principal seat; occasionally, however, it is distributed over the entire body. The palms of the hands and the soles of the feet become of a carmine tint when the skin is fair, as in the case of Europeans (Zülzer). The eruption, which may continue in convalescence, is often accompanied by burning and irritation which may cause sleeplessness; occasionally at the same time, swelling and painfulness of the cervical, axillary and inguinal glands set in, which however again disappear after

a few days. The eruption may last for a few hours only or between two and three days, and after its disappearance the patient becomes convalescent. Sometimes, however, it recurs after a day or two in another form.

Not rarely one of the two usual eruptions is lacking, and various authors such as Twining, Cawell, Mouat, Bimsenstein, Roux, and others, do not recognise an initial and a terminal eruption, holding that there is but *one*, which however may appear twice or thrice at short intervals.

The terminal eruption is mostly followed by a bran-like *desquamation*; this, however, does not appear at once after the eruption has vanished but only after the lapse of eight or ten days, and it lasts for two or three weeks. The desquamation is often so fine that the skin looks as if powdered. More rarely the epidermis falls off in larger flakes, as in scarlet fever. It is frequently accompanied by loss of hair, and sometimes followed by hyperæsthesia, more particularly of the palms of the hands and the soles of the feet, the latter occasionally remaining so tender that for a time walking is rendered difficult.

The *duration of the illness* is on an average six to seven days.

Convalescence is very slow ; general weakness, out of all proportion to the short duration of the attack, and articular pains, sometimes lasting for weeks or even months. The latter even may re-appear at irregular intervals for years. Often stiffness of the joints remains for some time.

Occasionally boils, carbuncles, abscesses and ulcers are observed during convalescence. In some cases there follow as sequelæ great sensitiveness of the stomach, obstinate intestinal catarrh, copious sweats, neuralgia, tedious deafness, aphasia, and intellectual disorders. Sometimes an intermittent fever accompanies convalescence and may last several weeks. According to Cotholendy this, however, always has to do with malaria.

The following ailments are mentioned as *complications :* pneumonia, pleurisy, pericarditis, nephritis, parotitis (which, however, but rarely ends in suppuration), swelling of the testicle, affections of the eyes (conjunctivitis, keratitis, iritis, irido-choroiditis, anæsthesia of the retina), ulceration of the mucous membrane of the mouth, persistent œdema of the hands and feet. In rare cases hæmorrhages are observed, most frequently from the nose and stomach, as also from the gums, throat, larynx, bronchial tubes, intestinal canal, urinary passages and uterus. In many cases severe menorrhagia sets in during the period of fever, and in some epidemics there are frequent miscarriages and premature births. Occasionally the hyperæmia of the skin attendant on the eruption is so severe that larger or smaller ecchymoses are left behind.

According to the degree in which the symptoms appear, severe, medium and mild forms of dengue fever can be distinguished. As sometimes one, and sometimes another symptom is more prominent, while others subside or disappear entirely, de Brun differentiates five different forms—the complete, gastric, the rheumatoid, the form characterised by the prevalence of headaches, and that form distinguished by the severity of the eruption. The mildest cases run an afebrile course, and in these the eruption may be the only symptom. The illness in very small children often appears in this form (Vernani). According to the observations made in Syria, it seems, as a rule, that the course of dengue fever in subtropical regions is milder than in the tropics, but of course there is considerable variety according to place and time.

It has been frequently observed that after the conclusion of the illness the entire process of disease is repeated. These *relapses* are doubtless not

due to a fresh infection but to a second development of the still extant virus of disease. In some epidemics these relapses are so frequent that they prove the rule. Originated by chills, over-exertion, errors of diet, &c., they mostly set in at the end of the first week, sometimes on the tenth or eleventh day, or even later. Occasionally the patients suffer with three or four such attacks, divided by intervals of fifteen to twenty-five days. In the relapses the fever is usually not so high, nor is the illness so intense as in the first attack.

The *termination* of dengue fever is, as a rule, a favourable one ; in some epidemics no case of death occurs, and in the severest the mortality does not exceed 1 per cent.

In 1872 there were 7,435 British soldiers in India ill with dengue, but only one died. Of 8,069 cases compiled by Martialis, 25 had a fatal termination.

The cases of death mostly occur in little children, aged people, or persons subject to severe chronic organic diseases (heart disease, tuberculosis, &c.). In children the cause of death is serious hæmatemesis, or convulsions ; in old people prostration or pulmonary or cerebral complications. In severe epidemics death has resulted from rapid hyperpyrexia, coma, and œdema of the lungs, or from sudden weakness of the heart and collapse at the time of the crisis.

An observation frequently made is that, with the recovery from dengue fever, the predisposition to other infectious diseases, such as typhoid, yellow fever, malaria, cholera, &c., is increased, so that it is not rare for attacks of one of the latter to follow soon after the former.

PATHOLOGICAL ANATOMY.

As the illness, as a rule, has a favourable termination, the opportunity for autopsies is but rarely afforded, and in the few cases in which *post-mortem* examinations were made, the conditions presented were not important. The changes found were : hyperæmia of the lungs and cerebral meninges, sero-purulent exudations into the meshes of the pia mater, serous effusions into, or in the vicinity of, isolated joints and into the pericardium ; pericardial adhesions and softening of the myocardium.

DIAGNOSIS.

The diagnosis of dengue fever presents hardly any difficulties. The ailments with which it may, under certain circumstances, be confounded are as follows :—

(1) *Acute articular rheumatism.* In the differential diagnosis it must be borne in mind that in this complaint there is no skin rash, and that the course of fever is dissimilar, no such rapid fall of temperature being observed in this ailment as in dengue fever. Also acute articular rheumatism never appears in epidemic form.

(2) *Scarlet fever.* In this illness the fever and eruption are of longer duration, and the pulse more accelerated than in dengue. Articular pains certainly appear in this illness, but do not, as in dengue fever, set in at the commencement of the illness, but only appear with the subsidence of the eruption, or the beginning of the desquamation.

(3) *Measles.* In this complaint, also, fever and skin rash are of longer duration. Furthermore there are no articular pains, while the

catarrhal symptoms, so prominent in measles, play a very subordinate part in dengue fever.

(4) *Influenza.* In this ailment the articular pains so characteristic of dengue fever are lacking, though neuralgia is frequently observed, while the catarrhal symptoms are more in evidence in influenza than in dengue fever. Skin eruptions certainly come under observation in influenza, but not nearly so frequently or in such variety as in dengue fever.

(5) *Acrodynia.* In the differential diagnosis between this and dengue fever, the most important factors to be taken into account are the afebrile course of the former, as also the localisation of the exanthem and the pains in the hands and feet.

Acrodynia has a few similarities with dengue fever. It is an illness[1] which has hitherto been observed in France, Belgium, Turkey, Persia, Algiers and Mexico in large and small epidemics. As to its etiology we are completely in the dark; it is probable, however, that it is originated by some alimentary lesion, like ergotism and pellagra. The illness begins with disorders of digestion, consisting of pains in the stomach, nausea, vomiting and diarrhœa; there is also conjunctivitis and an evanescent swelling of the face. After a few days swelling of and pricking or burning pains in the hands and feet set in, followed by hyperæsthesia spreading over larger areas. In other cases, or after previous hyperæsthesia, anæsthesia, particularly on the soles of the feet, sets in. Simultaneously with these symptoms an eruption, similar to exudative multiform erythema, appears on the hands and feet principally, but may spread further to the extremities, and occasionally even a few parts of the trunk are affected. In some parts the exanthem is marked by a dark discolouration of the skin. In serious cases spastic symptoms set in on the extremities, and if the illness is long-lasting there is emaciation of the affected limbs, as also local and general œdema. The illness, as a rule, has an afebrile course. The duration varies between a few weeks and several months, the long period being induced by relapses. Rarely, and then only in old and enfeebled individuals, is there a fatal termination, caused by long-continued diarrhœa. Convalescence, however, is always very slow and tedious.

PROGNOSIS.

The prognosis of dengue fever is in general a favourable one. There is a remarkable contrast between the benignity of the illness and the seeming severity of the symptoms. Only little children, old people, and sufferers from severe organic diseases are endangered.

PROPHYLAXIS.

In so benign an illness as dengue fever, added to the rapidity with which it is apt to spread and the general predisposition thereto, the carrying out of energetic prophylactic measures, such as the isolation of the patients, the barricading off of affected localities, establishment of quarantines such as have been recommended, would be attended with the greatest difficulty. It seems, however, feasible that individuals who, according to experience, are most endangered by dengue fever (little children, old people, sufferers from organic disease), should be protected in every possible manner from exposure to infection, so as to avoid all contact with dengue fever patients; it would therefore be best for them not to leave their dwellings during an epidemic.

[1] Hirsch's *Handbuch der Histor.-geog. Path.*, vol. ii., p. 173.

TREATMENT.

The treatment of dengue fever is *symptomatic*. Patients should keep their beds till the terminal skin eruption has disappeared and they feel well again.

At the *beginning of the illness* some observers advise the administration of an *emetic*, or a gentle *alterative* (a saline or calomel), or even an enema. V. Düring, on the other hand, urgently prohibits strong aperients.

High fever (40° and over) are combated by hydropathic measures (cold or tepid baths, cold irrigation, cold, wet packs), or by antipyretics (antipyrin, phenacetin).

During the *exanthematous stage* the administration of hot drinks is indicated.

Antipyrin has proved almost specific, according to Ornstein, for the *headaches* and *articular* and *muscular pains*. Inunction with liniments is advised to ease the pains in the joints. Sometimes subcutaneous injections of morphia have to be resorted to when the pains are particularly severe.

For *nervous excitement* and *insomnia* bromide of potash and chloral hydrate are administered, and for the *convulsions* of little children bromide of potash, cold fomentations and tepid baths are brought into requisition.

To allay severe *vomiting* pieces of ice and, if necessary, opium and morphia (subcutaneously) are given.

To relieve the unbearable *irritation* by which the patients are sometimes tortured, tepid baths, cold spongings, inunction with borax (10 in 30), chloral hydrate (2 in 100), or cocaine (2 per cent. solution or ointment) may be tried.

The *diet* of the patients must be light and nourishing.

During convalescence the use of tonics (iron, arsenic, quinine) is advisable. Persistent affections of the joints require massage, electricity, vapour or sulphur baths, or iodide of potassium.

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III.

YELLOW FEVER.

DEFINITION.

Yellow fever is an acute infectious disease peculiar to the warm countries of the Western Hemisphere. It is clinically characterised by a typical course of fever, great prostration, the appearance of icterus and albuminuria, and tendency to hæmorrhage ; anatomically the disease is characterised by an acute parenchymatous degeneration of the liver and kidneys and a fatty degeneration of the capillaries.

SYNONYMS.

Gelbfieber, Yellow typhus, Icteroid typhus, Black vomit, Fièvre jaune, Typhus amaril, Amarilisme, Typhus icterode, Pestilence hémogastrique, Gele Roorts, Vomito negro, Vomito prieto, Fiebre amarilla, Febbre gialla, Febris flava, Typhus icteroides, Febris ardens biliosa. (*Tyne.*)

HISTORY AND GEOGRAPHICAL DISTRIBUTION.

The earliest history of yellow fever is shrouded in mystery. It is unknown when and where the disease first appeared. The first positive information about this illness, according to Hirsch, dates from the middle of the seventeenth century, and originated with Father Dutertre, who in 1635 reported the disease from the Antilles. The Antilles are probably to be regarded as the *birth-place* of yellow fever, and from thence in the course of time it has spread further by means of human intercourse.

Yellow fever is a disease peculiar to *warm countries.* The geographical limits within which the illness has hitherto been confined are in the Western Hemisphere from 44° to 39° north latitude (Halifax), from 34° to 54° south latitude (Monte Video), and in the Eastern Hemisphere from 51° to 37° north latitude (Swansea), to 10° south latitude (Donde in Africa according to Hänisch).

Within this wide area there is, however, a relatively small region in which the disease reigns endemically, that is to say, where probably sporadic cases of yellow fever constantly occur, and from which from time to time (occasionally after decades of free intervals) an epidemic develops, without the illness having been brought in from outside. Such endemic centres are the West Indian Islands, more particularly Cuba

(Havana), a few spots on the coast of the Gulf of Mexico (Vera Cruz, Alvarado, Tlacotálpam, Laguna and Campêche) where yellow fever has become established in consequence of having been repeatedly imported; Brazil, particularly Rio de Janeiro, where this scourge has been endemic for thirty years; and finally a part of the Coast of Guinea (Sierra Leone). The last mentioned place has probably also been infected from the Antilles, and not the reverse, as stated by Pym; for the first reliable accounts as to the existence of this disease there do not extend back further than to the last twenty-five years of the eighteenth century (1778).

Beyond these districts, yellow fever occurs in the form of *epidemics* appearing periodically, and which can be traced back to having been carried in from its original home.

In North America it has been observed in all ports on the Mexican Gulf Coast, and on the Atlantic Coast as far north as Guayamas and on the Gulf of California. The most virulent epidemic experienced in the United States during the last century was that of 1878, in which 132 towns were visited by this scourge and to which about 16,000 persons fell victims. The latter epidemics, confined to a few of the Southern States, raged during the years 1897, 1898, and 1899.

In South America the geographical region of yellow fever extends to all the ports on the Mexican Gulf Coast and the Atlantic Coast south, as far as Monte Video and Buenos Ayres, from whence it extends to the Paranas as far as Corrientos and Assuncion, as also on the Pacific Coast from Mexico to Peru. It is only, however, since about 1860 that the disease has attained so wide a distribution. In 1849 it was carried to Brazil and even to Bahia by the North American brig "Brazil," which came from New Orleans, where the disease was raging. During the following year yellow fever was carried to Rio de Janeiro, and thence spread further along the coast and into the interior. Later on yellow fever was spread from Brazil to Peru, and to the States of Rio de la Plata. In Rio de Janeiro it raged from 1850 to 1861. In 1861 it was again imported to the same place from St. Jago and since then has kept a firm footing there.

Compared to the extensive region of distribution of yellow fever in the Western Hemisphere, its occurrence in the Old World is very limited. As above-mentioned, it was carried to Sierre Leone, where it is now endemic, and often appears epidemically north and south from this district on the West Coast of Africa and the West African Islands. Slight outbreaks were in 1895 reported from the Gold Coast (Accra and Coast Castle), and in 1899 from the Toory Coast (Great Bassam). In Cameroon, according to F. Plehn, yellow fever has never been observed. On the North Coast of Africa the disease has only once been noted, namely, in 1804, on the Island of Alhuzemas, off the coast of Morocco, whither it had been carried from Catalonia.

On the other hand, the South West of Europe, more particularly the south-west coasts of Spain and Portugal and Majorca, have been repeatedly visited by yellow fever. In Spain the first epidemic broke out in Cadiz in 1700, and several followed during the course of the eighteenth and at the commencement of the nineteenth century; these outbreaks spread over the greater portion of the coast, and even of the interior. Since 1821 Spain has experienced no severe epidemics, although the disease has several times occurred in limited areas. In Portugal yellow fever appeared in Lisbon for the first time in 1723, and a second great epidemic, extending also to other towns, was observed in 1856-1857.

Italy has only once had a transitory visit from yellow fever, and this was in 1804, in Livorno, where the disease had been carried from Cadiz.

Although ships having yellow fever patients on board have often entered French and British ports, no spread of the illness has taken place in consequence, with the exception of three small epidemics, which broke out respectively in Brest (Brittany) in 1856, in St. Nazaire (Brittany) in 1861, and in Swansea (Wales) in 1864. This scourge has never been observed in Asia and Australia.

The epidemic appearance of the illness *on board ships* which have come from infected ports is of special importance.

ETIOLOGY.

Yellow fever is caused by a *specific virus*, the nature of which is still unknown. It is my opinion that, though many observers have found micro-organisms in the blood, tissues and excreta of yellow fever patients and cadavers, and in spite of Sanarelli's *bacillus icteroides* which has called forth so much attention, the etiological factor of the disease has not yet been discovered.

The number of microbes observed in times of yellow fever and pronounced to be the cause of the disease is very great, and of which only Fiulay's " micrococcus tetragenus febris flavæ," Domingo Freire's " crytococcus xanthogenicus, or amarillus," Carmona y Valle's " peronospora luteæ," Da Lacerda's " cogumello fungus," and Gibier's and Le Dantec's " bacilli," need be mentioned.

Babès, who only had alcohol preparations at his disposal, found in the liver, as well as in the kidneys, chains of diplococci, which lay in ampullary sinuses of capillaries.

Sternberg, to whom the credit is due of having tested the bacteriological investigations of his predecessors by correct methods, found that most of the micro-organisms which he was able to culture from the blood, urine, evacuations, or organs of yellow fever patients or cadavers, were also to be found in the bodies of persons who had succumbed to other diseases, as also in healthy persons. In about half the cases he succeeded in cultivating from the *intestine* and *liver* a bacterium similar to the B. coli communis, which was, however, pathogenic to animals. This micro-organism he called bacillus X, and was of opinion that possibly it had some connection with the etiology of yellow fever. After the discovery of the bacillus icteroides by Sanarelli Sternberg identified his bacillus with that of Sanarelli, but subsequently convinced himself that he had been mistaken in this particular. Bacillus X undoubtedly belongs to the coli group.

Sanarelli's *bacillus icteroides* is a short rod (2-4 μ long) often appearing in pairs ; it is provided with rounded angles, and possesses four to eight flagellæ ; it is of a polymorphous character, is easily stained with the usual aniline dyes but not by Gram's method. Sanarelli found the bacillus in the *blood* and *tissues*, in the former during life also, but not in the stomach or intestine ; its numbers are always very limited, so that its isolation was very difficult, and as a rule it existed in company with other bacteria, such as bac. coli communis, streptococci, staphylococci, &c.

The bacillus icteroides may be *cultured* on the usual nutritive media. Its colonies on gelatine and agar-agar are very characteristic. On gelatine, which is not liquefied, the colonies during the first twenty-four hours appear as minute transparent drops ; later on they become whitish grey, and simultaneously a darker nucleus forms, which after five or six days turns black. Still later, the entire colony becomes black. Often the colonies are kidney-shaped. On oblique sterilised agar-agar the colonies have a different appearance, according as the growth is at 37° or at ordinary temperature. In the former case there is a smooth surface, in the latter case the colonies are button-shaped and vaulted. Should a culture, which had been kept at 37°, be placed at ordinary temperature, a luxuriant growth takes place round each colony. The smooth colony now appears surrounded by a prominent ring, so that it is not dissimilar to the impression made by a seal. The reverse occurs when cultures taken from ordinary temperatures are placed in the incubation apparatus.

The bacillus icteroides is facultatively anaërobic. It resists dessication to a great degree, being still found viable after 168 days. In moist heat it dies at 60° C. in a few minutes; exposed to dry heat it perishes between 120-125° C. It is killed by sunlight within seven hours. In sea water it remains viable for a remarkable length of time; to this circumstance Sanarelli attributes the obstinacy of epidemics in coastal regions.

The bacillus is transferable to *mice, guinea-pigs* and *rabbits*. The animals die of septicæmia after a few days, and pure cultures can be made from their blood and organs. In *dogs*, inoculations originate symptoms analogous to yellow fever in man, namely, vomiting, hæmorrhages from the stomach and intestines, albuminuria, and early death; anatomically degeneration of the liver, acute parenchymatous nephritis, and hæmorrhagic gastro-enteritis is found.

The blood serum of yellow fever patients agglutinates the bacillus.

A very strong *toxin* called *amaril* can be prepared by filtration from bouillon cultures fifteen to twenty days old, and this has the same effect as the cultures themselves. With this preparation Sanarelli experimented on five men (!); he originated the symptoms of yellow fever in them by subcutaneous and by intravenous injections. In one case the symptoms were very serious, but fortunately did not cause the death of the person experimented on. When heated to 70° C. the toxin remains unchanged, but if heated to boiling point its effect is considerably reduced. The relation of the bacillus icteroides to certain other microbes is peculiar. Streptococci, staphylococci, B. coli grow in abundance on nutritive soils on which the B. icteroides has been cultured. Therefore *mixed infections* are very common in yellow fever, and this explains the great difference and diversity of the forms of disease. Streptococci in great numbers are constantly found and, more rarely, bacteria coli and staphylococci are seen in the blood of dogs that have died in consequence of inoculations with the toxin. Moreover the development of the bacillus icteroides is encouraged by the presence of *mould fungi*, of which a special kind is noted, namely, the Sanarelli *aspergillus icteroides.*

If the impregnation of Petri's dishes has proved negative and they are allowed to remain until mould fungi develop on the same, it will be observed that simultaneously with the appearance of the dots of mould the bacillus icteroides in little points develop right round the colonies. The phenomenon is so constant a one that it may be utilised to force the growth of cultures that have remained sterile. The frequent occurrence of yellow fever on ships, especially old wooden ones, is explained by Sanarelli by the fact that ships with their holds, which are most difficult to clean, form a suitable soil for the development of mould fungi in the tropical zones, and in consequence for the development of the bacillus icteroides likewise.

Sanarelli believes that his microbe is introduced into the system by the medium of air and of water. He could transmit the disease to animals by the pulverisation of the bacteria. The microbes are not taken up by the healthy digestive tract. Persons newly arrived in the tropics are particularly prone to yellow fever, as they are apt to suffer with slight disorders of the stomach and liver, as the latter organ plays an important part in the disintegration of the bacilli which invade the blood, especially from the intestine.

Sanarelli's discovery has been confirmed by many other observers (Pothier, Hamilton Jones, Geddings, Foà, Gauthier, Mendoza, and others), but there are weighty grounds against the view that the bacillus icteroides is actually the cause of yellow fever. Sanarelli by no means always found this bacillus in every case of yellow fever, but only in seven cases out of thirteen—*i.e.*, in 58 per cent.—and always only in limited numbers. Similar disorders to those induced by him in man and beast can also be set up by various other bacteria. Furthermore the serum of healthy persons and animals, in about half the cases, agglutinated the bacillus icteroides, and in solutions of 1 in 20 (Norg). Although this bacillus is supposed to be contained in the blood, neither Sternberg nor other observers could succeed in infecting animals with the blood of yellow fever patients, even by the administration of large doses. In contradistinction to yellow fever, which requires a high temperature for its development (see below) the bacillus icteroides, according to Norg, can still grow at 10° C., and survives temperatures below 0° C. without injury. According to Reed and Carroll the microbe represents a variety of the bacillus of swine cholera, and only develops secondarily in yellow fever.

Havelburg found another *bacillus*, nearly related to the colon bacillus, in the *stomachic contents* of persons recently dead from yellow fever. The bacillus is exceedingly fine, small and straight (about 1μ long and 0.3 to 0.5μ broad); it often lies in pairs, and its pole is especially distinct. It is probably immobile. It is stainable with all aniline dyes but not by Gram's method, and exhibits no trace of the formation of spores. It grows on gelatine without liquefying it, also on agar-agar and in bouillon, on potato, serum, as also on acid nutritive soils, and it is facultatively anaërobic. It is specially

pathogenic for guinea pigs. If a culture of this bacillus be injected into a guinea pig, either subcutaneously or into the abdominal cavity, the animal dies, sooner or later, after paresis of the hind legs and convulsions have set in, and pure cultures of the bacillus are found in the blood. The same is the case when the stomachic contents of recent yellow fever cadavers are subcutaneously injected into guinea pigs. A previous injection of the blood of yellow fever patients into the abdominal cavity protects the animal from the effects of the cultural injections. If large quantities of blood are injected, however, it makes the animals ill and kills them. Havelburg, on the grounds of the protective effect of the blood, concludes that his bacillus is the specific yellow fever germ, and that there is a future for serum therapy in this disease.

Klebs in two cases of yellow fever found in the *liver* round and oval forms, which he considers to be *protozoa*. These he discovered by a particular method of staining ; they were partly in the hepatic cells, which exhibited degeneration in the form of vacuoles and deposits of fat, partly free, between the same or in the leucocytes which were mostly changed. These forms were also met with in the *stomach* and *duodenum* which, besides, contained forms of sporulation. Klebs regards yellow fever as a gastro-duodenitis, primarily originated by protozoa, and which attacks the liver, causing atrophy thereof, through the invasion by the parasites of that organ.

We do not know by what means the virus of the disease invades the body. It seems, however, certain that the transmission is not by means of drinking water. Yellow fever epidemics take longer to spread than is the case in cholera epidemics in which infected drinking water is the predisposing cause. When yellow fever occurs in a town with a universal water supply, one part may be spared while the other is attacked (Sternberg).

The *period of incubation* generally fluctuates between one and five days, the most frequent being between two and three days. The statement that, in rare cases, it may extend to several months, is to be regarded with grave doubts.

The virus of yellow fever does not seem to multiply in the diseased organism.

According to the present general opinion, the illness is not *contagious, it is not the yellow fever patient that infects but the yellow fever locality.* It has been observed times without number that patients taken to places free of yellow fever have never caused a single case of the illness, if the locality lacked the conditions necessary for the development of an epidemic.

The virus of the disease seems most particularly to cling to the *soil*. According to Nott's observations, in a house of several stories, those persons suffer most that inhabit the ground floor.

The virus of yellow fever can be CARRIED and widely diffused by *human intercourse or traffic and more particularly by maritime commerce.* Persons, healthy and sick, as also inanimate articles, such as clothes, &c., may serve as carriers of the virus of disease. Probably also insects (flies, mosquitoes) play a part in the dissemination of this disorder.

An observation communicated by Shakespear Allen proves that the virus of yellow fever may for a long time cling to *lifeless objects* and remain effective, *i.e.*, capable of propagation. In November, 1855, there died of yellow fever in Franklin, a woman who had unpacked a trunk containing bedding, and woollen and cotton goods, which had been packed away during the epidemic of the previous year, there being no other case of such illness in the town mentioned at this time. The Madrid epidemic of 1878 was traced back to the importation of the virus of disease through the medium of soiled linen and clothes. Between 17,000 and 18,000 soldiers returned from Cuba without one case of illness having occurred during the passage. About half of the troops were landed at Santander and despatched to Madrid with their baggage unopened. On their arrival their luggage was unpacked and cleaned, causing the outbreak of a small epidemic. The first persons attacked were a few washerwomen and stewardesses, whereas the soldiers, who were undoubtedly acclimatised, escaped the disease.

Further conclusions as to the qualities of the unknown virus of yellow fever may be formed from the general climatic and terrestrial conditions under which the illness appears.

A *high temperature* is necessary for the developement of the virus of yellow fever. The disease only rages throughout the whole year epidemically in tropical regions which at least have an average winter temperature of 20-22°C., but it prevails particularly during the hot and rainy seasons. In higher latitudes, with a winter temperature of less than 20° C., the illness only occurs in the hot season, and in places with a still cooler climate only during exceptionally hot summers. Yellow fever has never been known to gain a foothold at a temperature below 20° C. (Hirsch). Once an epidemic has set in, it may continue at a low temperature, but a considerable fall of temperature always causes an abatement and frost the extermination of the scourge ; this fact has frequently been observed on infected ships passing into colder latitudes. It has been repeatedly noted that epidemics which had been extinguished when the temperature fell to freezing point, revived in the following year without any fresh importations of the illness having taken place ; this occurred in Cadiz 1800-1801, in Malaga 1808-1809, and in Memphis 1878-1879. On board ship also it is possible that epidemics obliterated in consequence of frost, broke out anew as soon as the ship came under such climatic conditions as favoured the development of the virus, so that sometimes one importation of the disease on a vessel suffices to infect it for a long period.

A second, but less important factor in the etiology of yellow fever is formed by *atmospheric moisture* and *depression*, the virus requiring great moisture for its development. The prevalence of the disease in the tropics during the rainy seasons has already been referred to above. Even if epidemics occur during the driest season it must be remembered that such dryness is only relative. Copious and continuous rains often cause a cessation of the epidemic.

Yellow fever most often fastens on *certain localities*, more particularly *populous towns which lie on the sea coast or large navigable rivers, which in consequence of their position have a maritime commerce.*

The disease makes its appearance first in those parts of the town adjacent to the harbour and docks, where the sailors and dock labourers, and the newly-arrived foreigners, congregate, and which are mostly distinguished by their unhygienic conditions, caused by agglomerations of decaying organic matter which forms a favourable nutritive soil for disease germs. Single spots, single houses, flats, or single streets are always the foci of the disease, the neighbourhood being quite exempt. In Rio de Janeiro, which is severely afflicted with yellow fever, foreigners, though not acclimatised, are not often seized, for during the fever-period they live at Petropolis, which is hygienically situated at an altitude of 800 metres ; they only go to Rio during the day, and even then are mostly in the open air. Smaller towns and villages in the interior are but seldom visited by the disease.

Yellow fever is mostly confined to the *plains* and only exceptionally appears epidemically at higher elevations. Thus an epidemic was observed in Newcastle, Jamaica, in 1867, at an altitude of 1,200 metres. One also took place in Cuzco, in the Peruvian Andes in 1855-1856, at an altitude of 3,500 metres.

The reason for the immunity of mountains is, according to Hirsch, to be attributed to the lack of maritime commerce. This author says : " Yellow fever essentially does not spread beyond the limits of maritime

commerce ; the illness mostly reaches its limit where this medium of transmission fails." Still other circumstances, such as the low temperature of mountains, may be taken into account.

On board *ships*, especially wooden ones, in which the walls, utensils, ballast, and above all, putrid bilge-water, may be the carriers of the virus of disease, certain parts, such as a particular cabin, deck, or side, may by predilection be infected by the disease. Want of cleanliness plays a large part in the development of ship-epidemics, but only such ships are attacked as have had direct or indirect communication with other infected ships, or with an infected shore.

In countries where yellow fever is endemic, the virus of disease, during the epidemic-free season, is probably kept alive by a sequence of isolated cases. Outside the endemic home of the disease in order to cause an epidemic outbreak in a place, or on a ship, the following conditions, as stated above, must have co-operated : (1) Importation of the virus of disease through persons or inanimate objects ; (2) certain local conditions which favour the propagation of the germ ; (3) favourable meteorological conditions ; (4) the presence of persons predisposed to the illness.

From the time the illness has been imported until the outbreak of the *epidemic*, a period varying from a few days to many weeks may elapse ; the epidemic never sets in suddenly, it is always introduced by a series of single cases of illness ; it is only subsequent to such illnesses having existed for a longer or shorter time (four to eight weeks or more) that the epidemic usually quickly reaches its height. The first cases, as a rule, occur in the immediate vicinity of the imported case or infected ship. The severity, according to Touatre's experience, gained in New Orleans by the observation of the thirty-three epidemics there from 1847 to 1897, depends on the season in which they start. All those epidemics which began in August or September were slight, while those that broke out in May, June, or July were severe or of medium intensity. June, July, and August are the hottest months in New Orleans. The duration of the epidemics varies exceedingly, extending from a few weeks to several years. During the period remissions may alternate with exacerbations, these being caused by the influence of the weather or the movements of the population. The extinction of the epidemic may take place gradually, or it may occur suddenly, the weather having an influence on the disappearance of the disease.

Amongst a population attacked by an epidemic of yellow fever, there is a varying predisposition to the illness of which the following factors must be taken into account : —

(1) *Race and Nationality.*—Of all races, the *negroes*, even those not acclimatised in the yellow fever zone, possess the least predisposition. Negroes very seldom fall ill, and if they do the mortality amongst them is generally very low. According to La Roche, amongst the British troops in Jamiaca, 102 of the white men died yearly, and of the blacks 8 per cent. of the mean strength ; on the Bahamas the mortality amongst the whites averaged 59 per cent., and amongst the negroes 5 or 6 per cent. The *Mongolian races* also seem to possess a certain immunity ; this, however, is not the case with the American Indians (Red-skins) and the Hindoos. The *whites* run the greatest risks, the half castes less, decreasing as there is less white blood in their veins. Those born in higher latitudes are more susceptible than those born in tropical or subtropical regions. Of Europeans, therefore, the Russians, Swedes, British and Germans run far more risk of infection than the French, Italians and Spanish.

(2) *Acclimatisation.*—The susceptibility of whites who have emigrated

to the yellow fever zone diminishes with the time during which they stay there. It is also much lessened when they have gone through an epidemic without having themselves been attacked by the illness, and it is entirely extinguished by their having had and recovered from the illness. A second attack of yellow fever is of exceedingly rare occurrence. In the epidemic of Gibraltar in 1828, of every 9,000 patients only one case was actually proved to be a second attack (Louis according to Griesinger). The second illnesses are nearly always mild. The immunity gained by acclimatisation, by which foreigners as regards yellow fever, are placed in the same position as natives, only stands good as long as the persons to whom it relates remain in the region of disease, and is lost if they leave the same and return later on. The renewed acclimatisation, however, in that case would follow more quickly than in the case of a new arrival.

The relative immunity of *creoles* is partly a consequence of acclimatisation, and partly rests on the fact that creoles during childhood, especially the latter period thereof, have at epidemic times gone through more or less serious attacks of fever, which are to be regarded as mild attacks of yellow fever (Lota). Creoles who have been sent to Europe for their education are, on their return, as susceptible as if they had been born in Europe.

An observation made by Hegewitsch in Vera Cruz is interesting, as it would appear to credit the conjecture that *acclimatisation* is to be attributed to *metabolism*. According to this author, natives, old tropical residents, and those that have had yellow fever, are no longer stung by mosquitoes and other insects which are apt to worry new arrivals considerably (Hänisch).

(3) *Sex.*—The female sex is less liable to this disease than the male, and on an average the mortality is less. The probable reason for this is that women and children are less exposed to the danger of the disease than men.

(4) *Age.*—Yellow fever seldom occurs in children and the aged. The period between 10 and 30 years is the most liable.

(5) *Constitution.*—Strong persons are more predisposed to the illness than the weak and anæmic.

(6) *Environment.*—Persons living in insanitary environments are more liable to contract yellow fever than those better situated.

As regards occupation, labourers and sailors are most affected. According to Hänisch, those whose business brings them into contact with fire, such as cooks, bakers, sugar refiners, locksmiths, blacksmiths, are most liable to be attacked, while those whose occupations tend to the inhalation of unwholesome air, such as tanners, leather-workers, soap-boilers, tallow-chandlers, street-sweepers, &c., show less tendency to the illness. According to Souza Lima, cigar and cigarette makers seem to enjoy a certain immunity.

Infection by yellow fever seems to take place principally *at night*; persons who follow their occupations in the day in the town, but pass the night in Petropolis (situated on the hills near Rio), escape the disease in greater proportion than those sleeping at night in the town.

Incidental causes, as in other illnesses, are furnished by chills, bodily exertions, the influence of the direct rays of the sun, bodily exhaustion caused by tropical heat, especially if accompanied by much bodily exertion, sleeping in the night air, debauches, indigestion, exaggerated terror, sorrow, &c.

Yellow fever can also occur in animals, especially dogs and poultry, more particularly those that have been imported from Europe.

SYMPTOMATOLOGY.

Occasionally the outbreak of the actual illness is preceded by *prodromal symptoms*, consisting of general languor, headaches, giddiness, pains in the limbs, bodily stiffness, loss of appetite, belching, constipation and a dry skin. In most cases, however, the *onset of the illness* is *sudden*, commencing with slight chilliness alternating with heat, or a severe rigor lasting from fifteen to twenty minutes, followed by burning heat.

By predilection the commencement of the illness occurs during the night. The patients immediately feel seriously ill, and become quite dejected. A feverish restlessness develops, causing the patients to incessantly change their position and toss about in bed. There is but little sleep, and it is disturbed by terrifying dreams.

The patients complain of *vertigo* and severe *headaches*, particularly in the frontal and supraorbital regions. Pains in the loins (coup de barre) extend to the back, pelvis and legs ; the lumbar pains are associated with a sensation of weight and dragging in the testicles.

The temperature rises, and after a few hours averages 39° C. or more. The pulse is frequent and mostly small ; the respiration accelerated and superficial. The skin in serious cases feels dry and burning hot, but in milder cases there is a tendency to sweat.

The *face* is much reddened and swollen. The eyes ache and stream with tears, the conjunctivæ are severely injected and sometimes there is photophobia. In severe cases the eyes shine in a peculiar manner and the gaze is staring. Frequently herpes appears round the mouth and nose.

Sometimes in yellow fever other *exanthemata* appear, such as roseolas, urticaria-like eruptions, a pustular eruption, miliary spots, scarlet-fever-like and erysipelatous-like erythema. Bérenger-Féraud is of opinion that *erythema of the scrotum* is quite *pathognomic*. Touatre, on the other hand, who during thirty-three years in Orleans observed over 2,000 cases in nine epidemics, never saw the erythema mentioned.

The tongue is moist and swollen, red at the edges and with a white or yellowish coating down the centre. During the further course of the illness it often becomes dry and the coating assumes a dirty brown appearance. The mucous membrane of the palate is much reddened and swollen. The gums also become spongy and exhibit a tendency to bleed.

The appetite is quite gone. There is intense thirst, a *feeling of oppression* and great sensitiveness in the *region* of the stomach. Frequently pulsation in the epigastrium can be made out. Occasionally everything that has been eaten is at once vomited. The vomit is almost always sour, and sometimes it is mingled with bile. The bowels are constipated for the most part, but occasionally the evacuations are loose.

The *urine* is diminished, its specific gravity increased and its reaction almost always acid. The excretion of urea is considerably diminished, and to a less degree the uric acid also. Cunisset, in serious cases, only found 1·5 gr. uric acid (and still less) to the litre. Often, even at the beginning of the illness, traces of albumen are perceptible. According to Ruiz, Casabò and Cabello, the urine is supposed always, even during the

first few days of illness, to contain mucin. In serious cases, sometimes even from the commencement of the illness, there is more or less complete anuria. Occasionally, however, there is only retention present, so that the catheter must be brought into requisition.

The lungs and heart are not affected during the course of this disease, and the same holds good in regard to the spleen.

Already at the end of the first day or on the second day, the patient exhales a peculiar *putrid odour*. Stone and Woodville (1844) assert that they occasionally observed this smell even fourteen days previous to the outbreak of the illness. This odour is considered an untoward sign.
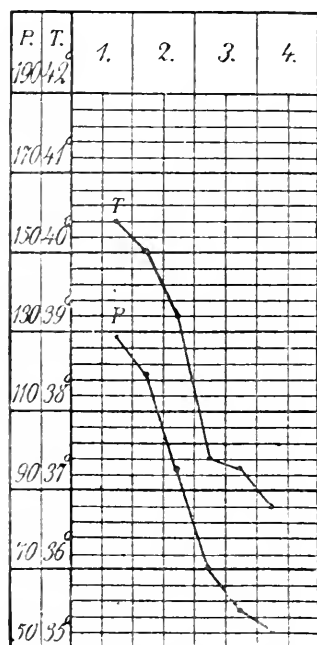
FIG. 7.—Yellow fever. Mild case.
Recovery.
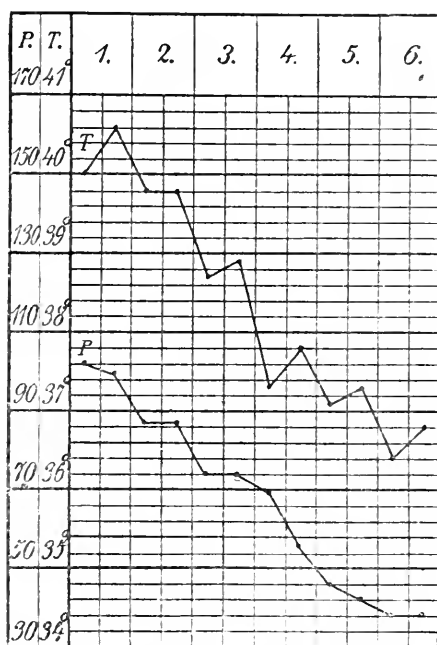
FIG. 8.—Yellow fever. Mild case.
Recovery.

During the two or three days following the invasion period an increase of all the symptoms takes place. The temperature in about twenty-four to thirty-six hours reaches its maximum, 40-41° C., only remaining so high for a very short time and then slowly or quickly falls, the fall being only interrupted by evening exacerbations. In rare cases very much higher temperatures occur. The highest temperature observed by Thornton was 42·2° C. ; by Nögeli 42·5° C., and by La Roche 43·3° C.

In mild cases the temperature rarely rises to 40° and the maximum is usually attained on the first day.

The fever usually lasts two or three days, sometimes longer. Death may occur during the first stage of the illness. Before death often a rapid rise of temperature takes place, this may continue after death, so that very high *post-mortem* temperatures (42·2-43·3°) are on record

(Sternberg). Roux in one case, shortly before death observed 49·5°. The pulse during the first stage is accelerated, full and hard. The frequency usually averages 100-120. The contrast between the pulse and the temperature is remarkable and considered by Faget and Touatre to be quite pathognomic. During the first three days, the number of beats, excepting slight variations, constantly decreases, even when the temperature rises. In mild cases, the temperature and pulse frequency fall in unison. Compare the accompanying charts taken from Touâtre's work (figs. 7-11).

Towards the end of the first period of the disease, or frequently only later, *jaundice* sets in. The sclerotics and the skin, more especially of the face, neck, and upper parts of the trunk, assume a hue which may
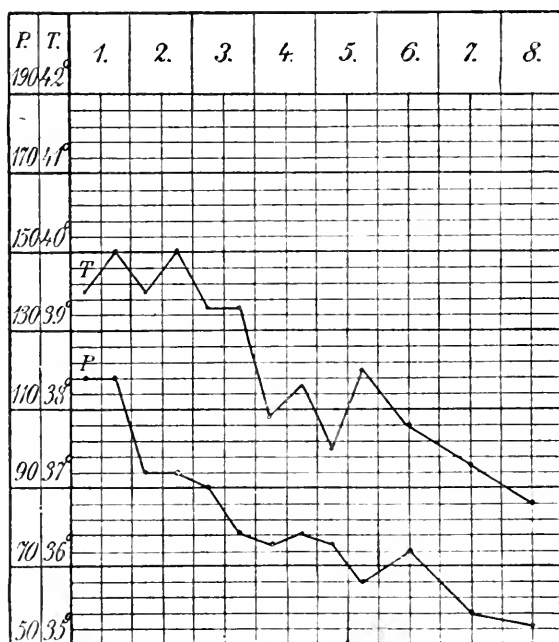
FIG. 9.—Yellow fever. Case of medium severity. Recovery.

exhibit every shade, from light yellow to dark orange, mahogany, or bronze-colour. Biliary pigment is sometimes to be demonstrated in the urine; bile acids, on the other hand are, as a rule, lacking. The fæces retain their biliary colouring and only quite exceptionally assume a pipe-clay appearance. The jaundice continues until convalescence sets in. Many cases, terminating fatally within two or three days, exhibit no icterus, the yellow tinge only becoming perceptible on the pale skin of the cadaver. In any case the icterus generally increases after death.

On the third day generally, a considerable abatement of nearly all the symptoms sets in and the patient passes from the first *stage of fever* into the *second*—the stage of *rest*. The temperature sinks and may become normal. The pulse becomes full and soft and its frequency decreases. The number of beats may fall to 40 or even 30 per minute. The skin

becomes cool and moist. The pains in the head and limbs abate. The patients feel subjectively better, their frame of mind is more tranquil, and they consider that the danger is over. The redness and swelling of the face disappear. The eyes lose their injection and their glare. Even the stomachic disorders abate though they do not quite cease. Though the urine may have contained no albumen in the first stage, albuminuria is almost always present in the second stage. In mild cases the quantity of albumen is small, in severe cases copious. According to Cunisset the albumen averages 0·2 to 0·6 per cent.

The duration of this period, which is only lacking in very rare cases, varies between a few hours and one or two days. In mild cases the second stage is immediately succeeded by convalescence ; the temperature,
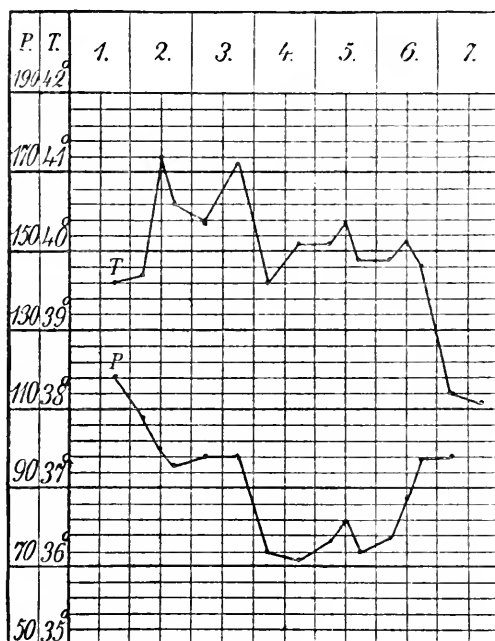
FIG. 10.—Yellow fever. Severe case. Death.

if not already normal, gradually falls and the other symptoms disappear quickly, so that the patient, after only a week, can resume his usual occupation.

More frequently, however, a change of all the symptoms for the worse sets in after the seeming improvement and the illness passes over into the *third stage* or *stage of collapse*. The temperature again rises, though not so quickly as at the beginning of the illness. The type of fever is more or less remittent. Sometimes the temperature sinks below normal, but this is an ominous sign. The pulse is sometimes accelerated, sometimes slackened, and usually small and threadlike. Consciousness is mostly maintained, but hardness of hearing or deafness, great apathy, and prostration are present. More rarely furious delirium sets in, the

features are pinched and distorted and the jaundice becomes very pronounced.

The patients again complain of pressure and intense burning in the region of the stomach. The *vomiting* which had abated again becomes more violent, or if none had existed previously, it now supervenes. At first watery material is vomited, later, in consequence of being mixed with blood, small blackish streaks are seen, and at last the vomit may assume a coffee-ground-like or quite black appearance. This is the much dreaded *black vomit* (vomito negro, Schwarz-brechen) which is considered a very unfavourable symptom, which, however, is not a constant symptom of yellow fever. It seldom appears before the third, usually on the fourth or fifth day. It is always a dangerous though not an absolutely fatal symptom. The vomiting of red blood, which is sometimes observed, is more to be feared.
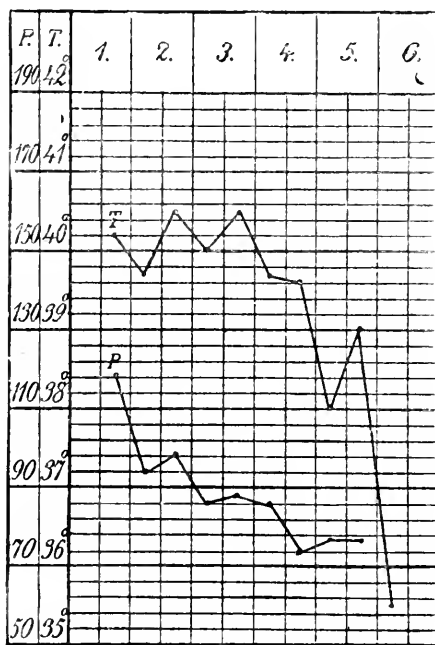
Fig. 11.—Yellow fever.　Serious case.　Death.

The black material vomited is, as a rule, odourless and shows a strong acid reaction. If allowed to stand it divides into a clear fluid and a black deposit. The microscope reveals the fact that it consists of blood, *changed by gastric juice.* According to Sternberg the microscopical examination exhibits numerous discoloured, or more or less deformed, red blood corpuscles, granulated leucocytes and orange-coloured, or yellowish-brown grains of pigment; Havelburg also proved the presence of blood. Cunisset could find no urea, gallic acid, or cholesterin in the vomited matters.

The *stool*, previously constipated, is now more or less loose. In fatal cases blackish masses, similar to those vomited, are passed ; incidentally pure blood also. Sometimes profuse diarrhœa with subsequent collapse sets in, so that a condition similar to the algid stage of cholera is met with. Frequently complete *anuria* is present.

Besides the hæmorrhages from the intestine and stomach mentioned above, many *hæmorrhages* in other organs occur, most frequently from the nose or mouth, beneath the skin and into the muscles ; more rarely the respiratory organs, the uterus, vagina, kidneys, bladder, urethra (if urethritis be present), eyes and ears, are the seat of hæmorrhages. Pregnant women usually, it may be said always during the first six months, *miscarry* (Nögeli) and few recover.

Jones, in two cases of miscarriage found the fœtus—one of four months, the other five to six months—also affected with yellow fever.

Death most frequently ensues in this stage, generally between the fourth and tenth day of disease. Consciousness may be maintained until the last moment, but most patients sink into a profound stupor. Often singultus, sighing and convulsive respiration, Cheyne-Stokes' phenomenon of respiration, and fibrillary muscular twitchings, precede death. If previously high, the temperature also sinks, sometimes even to 38°. In rare cases death sets in suddenly during violent delirium, or occasionally during convulsions.

Should the disease end in *recovery*, an occurrence which seldom takes place in advanced cases, a rapid fall of temperature often occurs, accompanied by profuse perspiration ; all the symptoms abate and gradually disappear. Convalescence is always protracted and drags on for several weeks. Sensitiveness of the stomach to all indigestible foods is especially apt to remain.

Occasionally convalescence is still further prolonged by secondary *complications* added to the original illness. Such are suppurative parotitis, buboes, abscesses, boils, cutaneous gangrenous inflammations, ulcerations of the scrotum, gangrene of the toes, hepatitis, diarrhœa, &c.

Relapses are, as a rule, rare in yellow fever ; they are more frequent in some epidemics than in others. They mostly set in during the first period of convalescence, sometimes two to four weeks after the disappearance of the fever (Sternberg). Relapses are often induced by excesses, especially indulging in copious drinks ; an error easy to succumb to as during convalescence great thirst is usual.

Besides the *perfectly typical cases* on which the above description of the illness is founded, and which as we have seen are again according to their course divided into *severe* and *mild*, other forms occur. These constitute the so-called *abortive cases*, such as generally also occur in other infectious diseases. In these cases there is no development at all either of icterus or hæmorrhages. After a stage of fever lasting a few days, perspiration and copious secretion of urine set in, and all symptoms rapidly abate. In other forms there may be an indication of icterus which generally, however, does not set in until all the other symptoms of disease have vanished and also the characteristic slowing of the pulse. Very mild forms are observed in Creole children.

Ambulatory yellow fever, like ambulatory typhoid, also occurs (Griesinger). The patients pursue their usual calling, but feel languid, have headache, dull injected eyes, pressure in the region of the stomach, constipation and lumbago. These symptoms last for about a week and gradually decrease, or during the course of an apparently trivial disorder an attack of vomiting of blood, followed by rapid collapse and death, may result.

On the other hand, cases are observed which are distinguished by a *foudroyant* course, and may cause death within the first thirty-six hours.

Apart from the severity of the cases there is no justification for dis-

tinguishing various forms of yellow fever. The differences exhibited by the separate aspects of the disease are only caused by differences of degree, or individual peculiarities and complications.

Finlay distinguishes three types: (1) the fever of acclimatisation, or yellow fever without albuminuria; (2) yellow fever with simple albuminuria, and (3) yellow fever with albuminuria and hæmatemesis.

Davidson cites as *pernicious*, the apoplectic, the algide, and the choleraic forms.

The *apoplectic* form begins suddenly with giddiness, followed by stupor, coma and convulsions, and it usually has a fatal termination.

The *algide* form is characterised by the early appearance of collapse. There is frequently a tendency to hæmorrhages, while icterus is often lacking.

The *choleraic* form is distinguished by profuse diarrhœas, severe vomiting, copious cold sweats, petechiæ and great prostration.

Yellow fever runs the same course in all countries, but the severity of particular epidemics is very different.

The percentage of *mortality* varies extraordinarily in the different epidemics.

Of the above-mentioned thirty-three epidemics in New Orleans, the mildest was that of 1897, the severest that of 1853; in the former the mortality averaged $\frac{1}{2}$ per cent., in the latter 85 per cent. In Senegambia, Roux even observed a mortality of 94 per cent. (of course the hospital conditions were bad). In this respect also the various periods of one and the same epidemic differ. Some epidemics begin with mild cases, and are followed by cases of great severity. In other epidemics the reverse is the case. Occasionally, during an epidemic, separate localities and streets of a town exhibit a remarkable malignancy of the fever. Finally, the mortality amongst the different classes of the population is unequal; whereas amongst the natives 7 to 10 per cent. is the average, the mortality may rise to from 20 to 80 per cent. amongst the non-acclimatised whites.

Death is most frequently caused by uræmia and cholæmia, more rarely by hyperpyrexia, abundant hæmorrhages, and insufficient hæmatosis.

PATHOLOGICAL ANATOMY.

In yellow fever cadavers the rigor mortis usually sets in early and is very pronounced, and the same is the case as regards *post-mortem* staining.

As a rule there is both cutaneous and *internal icterus* in varying degrees. The skin is, besides, occasionally the seat of petechiæ, or even ecchymoses, miliary spots, pustules, scarlet-fever-like, or erysipelatous inflammations, boils, carbuncles, ulcers, or gangrene; emaciation is mostly inconsiderable; hæmorrhages of different sizes are occasionally found in the muscles.

The *brain* and *cerebral meninges* are frequently hyperæmic, and more or less effusion is present in the ventricles and subarachnoid space; the effusion is sometimes turbid and of a yellow colour. The surface of the brain occasionally exhibits small punctiform hæmorrhages, and its surface, like the other organs, is of a pronouncedly yellow hue.

The *pericardium* often contains a large quantity of yellow or reddish fluid, and ecchymoses are occasionally found beneath the serous pericardium. The heart is frequently dilated, pale and flabby, its muscles showing fatty degeneration. In other cases these changes are absent. Crevaux, in 213 cases, found the cardiac fibres normal.

The blood is generally dark and fluid in the cadaver. Sometimes it has an acid reaction, sometimes it develops much ammonia. Its urea, according to Chassaniol and Cunisset, is increased. During the first period of disease the latter found $0.18-0.22$ gr., and after death $0.17-0.51$ gr. in 1,000 gr. standard, which, however, lie within the physiological limits.[1] In the second and third stage of the disease the blood contains biliary pigment. The red blood corpuscles are considerably diminished, and the white still more so. Sternberg, besides, observed very shiny granules which he considers to be fat, resulting from the disintegration of degenerated leucocytes.

The *capillaries* of the various organs exhibit fatty degeneration.

The *respiratory organs* are generally normal, but occasionally hæmorrhagic infarcts, ecchymoses beneath the pleura, and, in rare cases, larger serous effusions into the pleural cavity are found.

The *stomach and intestine* contain larger or smaller masses of black, thick or thin fluid, often tar-like, blood. The *mucous membrane of the stomach*, as a rule, exhibits the signs of acute catarrh with ecchymoses. Hæmorrhagic erosions are often found, but very seldom ulcers. In the œsophagus also erosions often occur, being probably a consequence of the corrosive condition of the vomit.

The mucous membrane of the small intestine often appears in a state of catarrh, and exhibits diffuse or patchy hyperæmia, a thick coating of mucus, swelling of the solitary follicles and of Peyer's patches, occasionally also extensive ecchymoses. The *colon* is generally normal. The intestinal contents have a more or less acid reaction (Sternberg).

Under the microscope Havelburg found the cells of the gastric and intestinal glands with parenchymatous clouding and fatty degeneration, with a simultaneous perishing of the glands. Hæmorrhagic areas are found between the glandular ducts, which can be traced to the surface. The epithelium is destroyed and transformed into finely granulated *débris* in the parts that are more or less diseased.

The *mesenteric glands* are always somewhat swollen and hyperæmic.

The *liver*, the changes of which are the most *constant* and *important*, is of normal size or but slightly enlarged, it is soft, and sometimes mottled yellow, sometimes yellow all over; when the course of the illness has been a rapid one it is plethoric, if of longer duration (six to eight days) it is remarkably anæmic. The hyperæmia more especially affects the branches of the portal vein, and is accompanied by œdema of the intralobular connective tissue. In drunkards the nutmeg liver is often met with.

Microscopic examination of the hepatic cells shows them to be the seat of cloudy swelling and fatty degeneration; the glands had almost disappeared. According to Havelburg, interstitial changes are not extant. Babès, on the other hand, found that the interstitial tissue was included in fresh proliferation and that the interlobular capillaries were much dilated, and in parts almost varicose.

According to Pellarin the hepatic tissue has lost its normal acid reaction, and is very poor in glucose and sugar; the bile is slightly alkaline.

The *gall bladder* contains dark, thick, viscid bile, or perhaps only a little mucus, or blood. The mucous membrane of the same is more severely injected and occasionally exhibits punctiform ecchymoses. The *biliary passages* are almost always free and permeable.

[1] Hoppe-Seyler, Physiologische Chemie, 1881, p. 431.

The *spleen*, in the majority of cases, exhibits no changes ; sometimes it is a little enlarged, hyperæmic, and soft.

The *kidneys* are somewhat enlarged and congested. Frequently small hæmorrhages are encountered beneath the capsule and in the cortical substance, which is sometimes enlarged, cloudy and of a greyish white colour. Microscopic examination shows turbid swelling, fatty degeneration, and desquamation of the renal epithelium, as also a more or less distinct obliteration of the malpighian bodies ; entire tubules, often without epithelium, are found filled and stopped up in places with different kinds of casts, especially of the granular variety. Babès also observed fresh interstitial changes.

The *pelvis of the kidneys* exhibits catarrh and ecchymoses, the same being often the case with the *bladder*. The latter is almost always contracted and empty.

Coagulated and fluid blood is almost always to be found in the *ovaries* and *uterus*, without menstruation having been present.

The most important anatomical changes, therefore, are the *icterus, the hæmorrhages of the different organs, the parenchymatous degeneration of the liver and the fatty degeneration of the capillaries and of the heart.*

We must conclude that the yellow fever virus exercises its deleterious effect principally on the liver, kidneys and capillaries. The diseased hepatic cells lose their capacity for retaining the bile formed in them ; and in consequence the bile flows into the blood and lymph, and icterus thus ensues (Liebermeister's akathektischer icterus[1]). The characteristic softness of the pulse in the second stage of the illness may be attributed to these, whilst the symptoms of the third stage are essentially due, partly to cholæmic, partly to uræmic influences. The hæmorrhages of the various organs are explained by the brittleness of the capillaries caused by fatty degeneration.

DIAGNOSIS.

No difficulties are presented in the diagnosis of yellow fever, when it is a question of well-marked cases occurring during an epidemic and within the more narrow regions of its home. The same cannot, however, be said in regard to isolated cases taking place beyond yellow fever limits. A differentiation between this disease and *icterus gravis*, which clinically, as well as pathologically and anatomically, may present an appearance exactly similar to yellow fever, is often remarkably difficult or quite impossible, depending solely upon the ætiology of the case in question, and the possibility of proving a connection of the illness with some yellow fever endemic or epidemic area. For the diagnosis of the mildest abortive cases, in which the characteristic symptoms of yellow fever are absent, the possible etiological factor during a decided epidemic is the sole distinctive guide.

The symptoms of yellow fever which should most particularly be taken into consideration for diagnostic purposes are : the sudden commencement, the remission after a few days, the lumbar pains, the reddening and swelling of the face, the injection of the eyes, the oppression in the region of the stomach, the albuminuria, the diminished or suppressed secretion of urine, the absence of the enlargement of the liver and spleen.

[1] *Deutsche medic. Wochensch.*, 1893, No. 16, p. 365.

Touatre lays great weight on the condition of the pulse during the three first days of disease (see above, p. 60), and for this reason it is necessary to narrowly watch the commencement of the illness. By carefully considering this symptom one will be in a position to avoid mistaking yellow fever for certain types of *malarial fevers* (*bilious remittent* and *blackwater fever*) as also for bilious *typhoid*, which present many symptoms in common with yellow fever.

Finally, the microscopical examination of the blood for distinguishing the diseases mentioned from yellow fever affords valuable assistance, by the presence of malaria parasites and pigment in bilious remittent and blackwater fever and of spirillum recurrens in bilious typhoid.

In mild epidemics also there is a possibility of mistaking yellow fever for dengue fever. For the differential diagnosis of these two diseases the clinical symptoms should be especially taken into account ; in yellow fever the pains are in the head and back, in dengue fever in the joints and muscles ; vomiting, frequent in the former, rare in the latter illness ; icterus usual in the former, exceedingly rare in the latter ; the condition of the urine, albuminuria and often anuria in the former, no remarkable changes in the latter ; an exanthem rare in the former, usual in the latter illness.

PROGNOSIS.

Yellow fever is always a serious illness, even seemingly mild cases sometimes quite unexpectedly assuming a severe aspect. The prognosis depends, first and foremost, on the severity of the epidemic, which may vary greatly in intensity.

The prognosis is generally more favourable in the case of women and children than in men ; it is unfavourable in patients over 50 years of age, and in drunkards, as also in persons enfeebled by excesses, insufficient food, &c. Touatre considers yellow fever less dangerous to children than measles, even the black vomit with them not being of the same importance as in the case of adults.

The *degree of the initial fever and the condition of the urine* are of great importance in prognosis. If the temperature rises to above 41° there is imminent danger to life. Should it rise to 42°, or even 43°, the fatal termination is unavoidable. Sternberg analysed 269 cases and found that in all cases in which the temperature rose above 41° death occurred. It is a favourable sign if 39·4°—39·7° are not exceeded during the first two days. It is considered a very unfavourable sign if no remission, or only a very slight one, takes place on the third or fourth day of disease. It is a bad prognosis if there is great decrease or entire suppression of the secretion of urine ; a large quantity of albumen in the urine is likewise a bad sign.

Severe and protracted injection of the eyes, the early appearance of icterus, severe stomachic disorders and frequent vomiting, the appearance of black or red vomit (in the latter death is almost certain)—all these are *unfavourable signs*, as also are hæmorrhages from the intestine, or into other parts, especially if connected with algide evacuations (always excepting slight bleeding from the nose at the commencement of the illness, which is considered benign), the appearance of delirium, singultus and sighing respiration.

PROPHYLAXIS.

The prophylaxis of yellow fever is divided into *general* and *personal* prophylaxis.

General prophylaxis consists partly in preventing the increase of sporadic cases and the occurrence of epidemics in those particular countries in which yellow fever is endemic, and partly in taking measures to avoid the disease being carried into ports exposed to the danger thereof.

As to the former, it is to be effected by *improving the hygienic conditions* by removing heaps of decayed organic matter, by thoroughly cleaning the streets, and having the dwellings kept clean, in order that the virus of yellow fever be deprived of a soil suitable for its development. The same measures should be taken in towns exposed to the danger of the illness being imported.   On board ships epidemics of this disease should be prevented by cleanliness and good ventilation.

As yellow fever is principally carried by maritime commerce, all ships and goods exposed to infection should be controlled by strict sanitary police supervision.   Ships having, or having had, yellow fever patients on board should be placed in *quarantine*.   As the period of incubation of yellow fever is not usually longer than three to five days, a quarantine of five days would suffice.   During winter it appears unneccessary in ports in the more northern areas to have quarantine, for in cold weather there is no danger of the development of an epidemic.

In the United States there is a fixed law that all ships hailing from Central and South America, having on board cases of yellow fever or cases suspected to be yellow fever, shall, during the hot season (May 1 to November 15), be placed in certain quarantine stations, as shall also all ships coming from the West Indies.   In these stations the ships have to submit to the regulation treatment before they are allowed to enter other North American ports.

Patients should be isolated in *quarantine hospitals* and their *soiled linen* and *clothes* should be *disinfected*, as should also the *ship* itself and the clothes worn by the healthy crew and passengers.   Ships that have had communication with infected ports or ships, but that after a subsequent long voyage have had no case of illness on board, need not be quarantined, but the usual disinfection must be undergone.

If yellow fever has been carried into a seaport town, the centre of infection must be limited as much as possible by the *isolation of the patients* and the *disinfection of their dwellings*, by *compulsory reporting of every case of the illness*, and by *strict house to house inspection* for the discovery of cases that might possibly be hidden.

Although it has not been proved that the evacuations (urine, fæces, vomit) of patients contain the virus of yellow fever, it is advisable to disinfect these likewise.

In order to prevent the illness being carried further into the interior, a land quarantine must be established.   The measures taken by the United States, as described by Cochran, may well serve as a model. After the appearance of yellow fever in a seaport town every regular connection with the infected spot during the period of the epidemic is closed.   Neither persons nor goods may leave the district except in special trains and under special supervision.   The regular passenger and goods trains are not allowed to stop at or near the infected town, so that nothing infectious can be put on them.   The particular trains which carry all the persons who wish to leave the infected town start as often

as circumstances require, and convey the refugees to such places beyond the yellow fever zone as are inclined to receive them. The trains of the refugees are only permitted to stop at small stations to obtain necessaries, such as water, fuel and food. Those refugees who have come from infected localities and have been exposed to the danger of contagion are obliged to betake themselves to certain " camps of probation," where they have to undergo a ten days' quarantine, and where their luggage is disinfected.[1] Those persons remaining behind in the infected town under the shadow of the scourge, are likewise provided with necessary stores by special trains. Of course it is understood that already with the first appearance of the illness, and before any quarantine measures have been adopted, many persons take to flight unsupervised.

In regard to *personal prophylaxis*, those who are predisposed to yellow fever should avoid any communication with infected places, persons and things, and if anyhow able should leave the town affected with yellow fever. Should this be impossible, one should sleep as high as possible above the ground ; excesses of all kinds, especially of drink, should be avoided ; one should be protected from the sun during the heat of the day, and take care to avoid chills after bodily exertions and keep the bowels open ; in fact, one should avoid all injurious habits which according to practical experience act as predisposing causes (see above, p. 57).

Domingo Freire, in Brazil, and Carmona y Valle, in Mexico, have recommended and carried out *protective inoculations*, the former with weakened cultures of his cryptococcus xanthogenicus, the latter with the residue of the urine of yellow fever patients ; these, however, proved of no value, being based on erroneous principles (see above, p. 52).

Finlay *recommends protective inoculation by means of gnats.* His procedure is as follows. Young gnats are caught in little bottles, or test tubes, in a house free from yellow fever, then applied to the freshly-washed skin of the breast or arms of a patient who has not been ill more than six days. When the gnats have sucked their fill they are taken off and two to five days are allowed for quiet digestion.

With these gnats inoculations are carried out, the same being placed on the skin of the persons to be inoculated. The gnats immediately bite, whereby contagion ensues. Finlay, by this method, inoculated 100 persons between 1881 and May, 1895, of whom, during the course of the following year, 43 had mild attacks of yellow fever, 9 severe attacks, and 3 died. Amongst those inoculated there were 76 friars. During this time 5 non-inoculated friars, of a total of 37, succumbed to this disease.

TREATMENT.

The treatment of yellow fever is *symptomatic ;* hitherto no specific remedy for the disease has been discovered.

At the beginning of the illness an aperient is given, either calomel or castor oil. Of the former 0·5—1·0 is given for a dose, of the latter 3·0—60·0. Rush advises calomel mixed with jalap (āā 0·7). Roux recommends sulphate of soda or magnesia with senna. If necessary the alteratives are several times repeated during the course of the illness. Touatre advises the use of two enemas daily, consisting of warm water, with sulphate of soda or magnesia one teaspoonful to half a pint.

A *diaphoretic treatment* is also recommended at the commencement. Hot footbaths containing plenty of mustard are given, whilst the patient, with his chair and bath, are wrapped in a blanket from head to foot. This may be repeated several times during the first twenty-four hours.

[1] *Veröffentl. des Kaiserl. Gesundheitsamtes*, 1893, No. 37, p. 694.

Priessnitz's packs are also applied, while hot tea is imbibed.   Baths as hot as can be borne are ordered, the patient being subsequently wrapped in blankets for several hours.

The *fever* is most successfully combated by *hydropathic methods*, such as cold water bandages or ice bags on the head, repeated cold sponging of the upper part of the body or of the whole body, cold packs, tepid or cold baths.   Da Silva Ramos recommends very short cold baths ; the patients are immersed for a few moments in a full-length bath filled with water of 10—12°.   This is supposed to be followed by quiet sleep, stronger action of the heart, deeper respiration, and an increase of the secretion of urine.   The baths are repeated after a few hours, if the symptoms have again increased, and six such baths may be given within twenty-four hours.   *Febrifuges* have lately also been much used, especially antipyrin and phenacetin.

The exceedingly acid reaction of the vomit has led to the belief that an acid diathesis prevails in yellow fever, and in consequence to an *alkaline* treatment of the illness in all its stages.   As early as 1867 bicarbonate of soda was recommended by Stone.   Sternberg adds sublimate to the same (soda bicarb. 10·0, hydrarg. perchlor. 3·02, aq. 1000·0 ; of this 50·0 [three tablespoonsful] are to be taken every hour ice-cold).   This formula is known as " *the Sternberg* treatment."

By this treatment Sternberg reports that of 301 whites thus treated only 7·3 per cent. died ; and amongst 73 blacks attacked there were no deaths.

Touatre, who is opposed to the administration of any drugs internally in yellow fever, advises that copious draughts of alkaline *Vichy water*, if necessary ice-cold, should be drunk.

Foreman and Anderson recommend *carbolic acid* (up to 0·2 daily), the latter in an alkaline effervescing mixture ; Wallbridge orders sulphocarbolate of soda ; Freire salicylate of soda (1·0 or 2·0 dissolved in four parts of distilled and sterilised water subcutaneously, or 4·0 to 10·0 internally) ; Liénas prescribes *liquor ferri perchlor.* (20 to 40 drops during the course of the day).

To relieve the *lumbar pains* dry cupping, sinapisms and blisters are used ; sinapisms and blisters are also used to allay the *vomiting*, as also hot poultices in the region of the stomach (Corre).   For the same purpose small pieces of ice may be swallowed, and morphia, especially subcutaneously, chloroform (a few drops on sugar) and cocaine are used. Blair sounds a note of warning against large doses of morphia, as he has observed bad consequences even after 0·006.   Thorington gives 0·02 cocaine ten to fifteen minutes before drink is taken, and if the vomiting does not cease he gives half the quantity every hour until it abates.

When *blood is vomited*, i.e., *black vomit*, bits of ice should be given to swallow, an ice bag applied over the region of the stomach, and styptics, such as liquor ferri perchlor. (15·0 to 1000·0 water and sweetened with sugar, a tablespoonful every hour), ergot, ergotin, acetate of lead with opium, may also be tried.   The latter should also be given for other hæmorrhages.   Otero is of opinion that cocaine is a more effective hæmostatic than any other styptic.

To allay the *nervous restlessness* and *insomnia*, sedatives of the coal tar product type, such as antipyrin and phenacetin, are given (Cochran).

For *collapse* stimulants, especially alcoholic, should be given, according to the idiosyncrasy of the respective patients, beer, porter, whisky, wine, champagne or camphor ; æther subcutaneously is also indicated.   Corre recommends digitalis.   Hot water bottles and hot blankets are also useful.

When the skin is hard and dry and the urine scanty, and lumbar pains are present, Sternberg prescribes pilocarpin subcutaneously.

The *nourishment* of the patient is of particular importance. During the first days this should be confined to liquids, such as milk (under some circumstances buttermilk and sour milk) and broth. When the stomach is very sensitive limewater (one tablespoonful to a cupful) should be added to the milk. When there is severe vomiting, iced milk, iced champagne or brandy (one teaspoonful every half hour) should be given. If even these cannot be retained nutritive enemata must be resorted to. As soon as the stomach can again retain food, a light digestive diet should be given to the patient. Errors in diet must be strictly avoided.

Sanarelli immunised horses by means of bouillon cultures of his bacillus icteroides, and gained from them a *curative serum* to which immunising as well as curative qualities are attributed. As, unlike diphtheria curative serum, it is not anti-toxic, but has a bactericidal effect, it must be used during the first two days, at the latest on the third day. The quantity which should be injected under the skin of the thigh, buttock, and in urgent cases into the veins of the forearm, averages 20 ccm.; if necessary the injection may be once or twice repeated. The propitious effect of the serum is indicated by an increase of the secretion of urine, and often by actual polyuria.

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IV.

MEDITERRANEAN FEVER.

DEFINITION.

A specific infectious fever, endemic, and sometimes epidemic, on the coasts and islands of the Mediterranean, is designated *Mediterranean Fever*. Clinically, this illness to some extent resembles typhoid; but it is distinguished from typhoid by its long duration, sometimes extending over many months; by a course of fever exhibiting marked undulations; by the occurrence of copious perspirations; by the frequent appearance of rheumatic articular disorders, as well as by neuralgia and inflammation of the scrotum and epididymis.

SYNONYMS.

Mediterranean fever, Malta fever, Gibraltar fever, Rock fever; Neapolitan, Cretan, Cyprus, Levant, &c., fever, Gastric remittent fever, Bilious remittent fever, Intermittent typhoid fever, Typho-malarial fever, Fœco-malarial fever, Sewage fever, Mephitic fever, Cesspool fever, Undulant fever; Fièvre typhoide sudorale italienne; Febbre gastro-biliosa, Febbre tifoidea atipica, Pseudo-tifo, Febbre infettiva atipica; Febris sudoralis, Febricula typhosa, &c.

HISTORY.

The history of Mediterranean fever can be definitely traced back to the commencement of the nineteenth century. At this period it was first mentioned in the sanitary reports of the British army and navy, but it was only after the Crimean war that it was distinguished from typhoid and malarial fevers. It was first described by Marston in 1859 as a *specific* illness.

GEOGRAPHICAL DISTRIBUTION.

As its name indicates, Mediterranean fever occurs on the *coasts* and *islands of the Mediterranean Sea*. It is especially observed in Gibraltar, and in Malta, where the British soldiers and sailors, and also the natives, suffer from the illness. It appears, moreover, in Algiers, Tunis, Sicily, Sardinia, Naples, and other towns on the coast of Italy, as also in Crete. Its occurrence, however, is certainly not confined to this region. The illness is to be met with, not only in Constantinople, on the banks of

the Danube, and on the coast of the Red Sea (Suakim, Massowa), but it is probably also widely distributed over the tropical and sub-tropical countries of the East, where it is still confused with typhoid, remittent malarial fever and continued fever, or has even been called typho-malaria. Buchanan describes a form of fever occurring in Indian jails which exhibits great similarity to Mediterranean fever. Wright and Smith, by means of the serum diagnosis practised on soldiers who had returned home, were able to substantiate the occurrence of the illness in northern India. It is probably also endemic in China (Hong Kong) and America (Puerto Rico).

The form of fever described by Buchanan appears during the "unhealthy" season. The fever is not high, may be continuous, remittent, or even intermittent, and lasts ten to fourteen days. An afebrile interval of about an equal period follows, then fever again for a week or longer. Three or four relapses are not unusual, so that the illness lasts ninety or even one hundred and twenty days. The illness runs its course almost without definite symptoms, the spleen being only occasionally enlarged. The appetite remains good for weeks, and the bodily weight does not diminish quickly. Buchanan has never found malaria parasites in this illness.

ETIOLOGY.

Mediterranean fever was formerly regarded as a peculiar form of typhoid (Wood, Borelli) or as a combination of typhoid and malaria (Maclean, Notter, Milnes). It is only lately that it has been recognised as a specific disease, especially after Bruce succeeded in Malta, in 1887, in demonstrating a certain *micro-organism* which may be looked upon as the genesis of the illness. The micro-organism referred to is a very small round, or nearly oval, micrococcus of about $\frac{1}{3}$ μ diameter, and which is often seen united in couples, and sometimes in chains of four. It is possessed of no spontaneous movement and can be readily stained with gentian violet and methylene violet, but not by Gram's method. It is contained in the *spleen* and *liver* in great numbers, probably also in other organs. Bruce found this micro-organism, which he called *micrococcus melitensis*, in twelve out of thirteen cases of Mediterranean fever examined, while cases of typhoid simultaneously examined in Malta never lacked the typhoid bacillus in cultures; the same micrococcus was confirmed by Hughes in fourteen cases of Mediterranean fever with a fatal termination. The micrococcus can be artificially cultured and the disease can be trans-mitted to animals by pure cultures.

Gordon observed spontaneous movement of the micrococcus melitensis, and by means of van Ermengem's method of staining (modified), he was able to demonstrate a flagellum, more rarely two to four.

The micrococcus melitensis, which is distinguished by a slow growth, thrives best on a nutritive soil, the alkalinity of which is somewhat less than that of human blood, and at a temperature of about 37° to 38°. Between 40° and 42° and at 18·5° its growth ceases, and at over 42° it dies off, as it does also if kept long at 15·5°. It withstands desiccation for some time.

Meat peptone (*agar* 1½ per cent.) proved the best nutritive soil for the micrococcus melitensis. Plate cultures were not successful, but puncture cultures and cultures on oblique sterilised agar succeeded. In *puncture cultures* pearly-white areas round the punctured spot develop after a few days, and small, round, white colonies form along the line of puncture. After a few weeks the colonies on the surface become larger, and form rosette-shaped cultures, and along the line of puncture a solid rope of yellowish-brown colour with serrated processes has developed. After a few months the cultures acquire a tan colour.

On *oblique sterilised agar*, round, slightly raised, smooth, shiny colonies with even outlines develop after nine or ten days and are about the same size as small shot No. 4. On holding the same up to the light the centres of the cultures appear yellowish and the

peripheries bluish-white; in a reflecting light they appear milk-white throughout. Their growth is very slow; even after a couple of months they are not larger than hemp seeds.

On *gelatine*, the micrococcus at 22° shows but a slight growth without liquefying the gelatine.

No growth takes place on *potatoes* at the temperature of the body.

Bruce and Hughes made *experiments* in regard to *transmission ;* they used pure cultures subcutaneously injected, but they only succeeded with monkeys. The latter contracted fever analogous to that of Mediterranean fever patients, and recovered after from eleven to thirteen weeks, or died after only from thirteen to twenty days. At the *post-mortem* examinations pathological-anatomical changes similar to those in man were found, and the same micrococcus could be again cultured from the organs. Durham, Wright, Semple, and others succeeded also in infecting rabbits and guinea-pigs by intra-cerebral and intra-peritoneal injections. Latterly, also, two successful inoculations (one unintentional and one intentional) were observed in the pathological laboratory at Netley in the case of men, whereas the experiments on negroes, conducted formerly in this direction by Bruce, yielded negative results.

The blood serum of sufferers from Mediterranean fever and monkeys that had been inoculated with micrococcus melitensis, had an agglutinating effect on pure cultures of the latter (Wright).

Mediterranean fever is *not contagious*. The introduction of the virus takes place by way of the air passages or intestinal canal; it is probably also taken in with drinking water or food.

The *period of incubation*, according to Birt and Lamb, varies from eight to twenty days, fifteen days seem to be the average time, however.

The development of the disease is favoured by *hot, dry weather ;* it therefore is principally observed during the summer months. The greatest number of cases, according to Hughes, occur between May and the middle of October, the fewest between November and April.

Unfavourable hygienic conditions, especially contamination of the soil by human excrement, seem to play an important part in the development of the disorder. The etiological factor of disease is probably evacuated with the urine and fæces, these reach the soil, and are thus transmitted to the air and drinking water. In Malta, as stated by Hughes, Mediterranean fever appears principally in the old buildings erected by the Knights of Malta, which were always overcrowded and unhealthy; it also occurs on board ships at anchor in Malta harbour. The author attributes the latter incident to a contamination of the harbour water, which is used for bathing and with which the ships are washed.

Lately, Mediterranean fever in Malta has become less frequent, probably in consequence of improved hygienic conditions. According to Hughes, in 1859 269·5 per cent. of the British soldiers suffered from the disease, but in 1888 only 71·2 per cent.

Sex has no predisposing influence on the illness, and every *age* is prone to be attacked, but mostly that between 6 and 30. Natives fall ill more rarely than strangers, but acclimatisation plays no part in this ailment.

As *incidental causes* the usual detrimental influences such as chills, bodily and mental exertions, excesses, &c., may be quoted.

Immunity is acquired by having once gone through the illness. The immunity is, however, not always absolute but may be again lost after some time (Hughes).

SYMPTOMATOLOGY.

The illness begins with the usual symptoms of fever : loss of appetite, indisposition, rigor, headaches, mostly localised in the forehead, moreover, pains in the limbs and loins, and sleeplessness. The tem-

perature rises gradually, and generally attains its maximum after several days. The face, in severe cases, is reddened, the patient looks excited and complains of tinnitus aurium. Sometimes nose-bleeding occurs at the onset of the illness. The tongue is at first swollen and thickly coated, and in severe cases it becomes dry and fissured and bleeds readily during the further course of the illness ; the gums become relaxed, bleed easily, and are in a scorbutic condition. The pharynx has frequently a reddened appearance, and is occasionally ulcerated. The tonsils are often enlarged. With these symptoms there is loss of appetite, nausea, occasional vomiting, and a feeling of oppression and sensitiveness in the region of the stomach. The bowels, as a rule, are constipated. Occasionally, mostly after errors in diet, diarrhœa sets in, with or without pain in the cæcal region. The evacuations are dark and of offensive odour, and sometimes are of similar consistence to those occurring in typhoid. The stools at times exhibit a mucous and bloody composition. Occasionally the abdomen is distended with wind, causing gurgling in the cæcal region. The spleen is enlarged, as also the liver to a less degree, and both organs may be sensitive to pressure. Sometimes there is slight icterus, and nearly always more or less severe bronchitis, often accompanied by expectoration streaked with blood. In rare cases pneumonia is observed, which, according to Notter, always has its seat on the left side and is accompanied by pleurisy. As a rule the patients complain of palpitation in the region of the heart. Generally there is great, it may even be said profuse, secretion of sweat, which mostly sets in about 1 or 2 in the morning, and in consequence sudamina always form, more or less ; the illness has in consequence been designated *febris sudoralis.* A skin rash has never come under observation. Consciousness is generally maintained, but sometimes, during the nights especially, slight delirium sets in.

After from one to three weeks all the symptoms abate, the temperature gradually falls, and the patient considers himself convalescent. This improvement, however, is not maintained. After a few days a relapse sets in, the temperature again rises, the former disorders recur, and weakness, apathy and emaciation increase, while the complexion assumes a pale, clay-coloured hue.

During the further course of the illness *rheumatoid articular affections* are observed, according to Bruce, in about half the cases. One or more joints become painful and swell, and the skin over the joint is reddened. According to the same author the shoulder, knee, and hip joints are most frequently attacked, but sometimes all the joints are affected. Painful swellings also of the bursæ and of the periosteum are observed. In gouty subjects the beginning of the illness may be accompanied by a typical attack of gout.

Neuralgia may develop in almost any part of the body, but sciatica is especially prone to occur.

In rarer cases *epididymitis* and *orchitis*—generally one-sided—sets in, and after a few days again vanish. Mastitis is very uncommon.

Occasionally, also, partial anæsthesia or hyperæsthesia, particularly on the soles of the feet, have been reported, and, more rarely, paralysis and atrophy of single muscles, such as the deltoid, the flexors of the foot, &c., with the tendon reflexes maintained or even increased. Moreover, hardness of hearing sometimes occurs.

In later stages of the disease skin eruptions are not uncommon, such as erythema, eczema, erythema nodosum (Notter). Occasionally also purpura accompanies the hæmorrhages above mentioned (bleeding

of the nose, hæmorrhage from the gums, hæmoptysis). At about the fourth week desquamation of the skin, especially from the soles of the feet, sets in, the skin dropping off in large pieces. Sometimes also the hair of the head falls off.

Albuminuria is of exceedingly rare occurrence.

The symptoms, as regards the respiratory organs, are frequently so pronounced that, in view of the presence of profuse night sweats, Mediterranean fever may be mistaken for phthisis. The older authors used frequently to mention *Mediterranean phthisis*, and state that it usually had a favourable termination.

The duration of Mediterranean fever varies; in the mildest cases in which, with the exception of fever with temperature of from 39·5° to 40·0°, there are no further symptoms of disease, it averages from two to three weeks. Mostly, however, relapses occur, these being characteristic of the illness. Periods of fever lasting several days or weeks are followed by periods of days or months during which the temperature is normal, or, more frequently, only a little above normal ($\frac{1}{2}$ to 1°), then again periods of fever set in, and thus the disease may drag on weeks and months; according to Bruce it may even continue for two years. Hughes gives ninety days as the average stay of the patients in hospital. As the illness goes on the length and intensity of the periods of fever diminish, the fever being apt in the earlier stages to exhibit a continuous and in the later stages a remittent type. Compare the temperature chart taken from Hughes' monograph (fig. 12).

On account of the marked undulations exhibited by the charts in Mediterranean fever, Hughes has appropriately called the illness *Undulant fever*. It, however, may also happen that the fever continues for months without interruption, during which period temperatures of 40·5°, 41·0° and even higher are observed.

In most cases Mediterranean fever has a favourable termination. The fever gradually diminishes and no new relapses set in.

A long time, however, elapses before the exhausted sufferers recover, and for months after the illness there is a tendency to neuralgia and articular and scrotal swellings, with slight fever. Young and much enfeebled persons sometimes develop pulmonary phthisis or other severe affections of the respiratory organs subsequent to their recovery from Mediterranean fever (Maclean).

A fatal issue mostly occurs during the first four to six weeks, and is usually caused by hyperpyrexia. Shortly before death a consider-

Fig. 12.—Mediterranean fever. Undulant type.
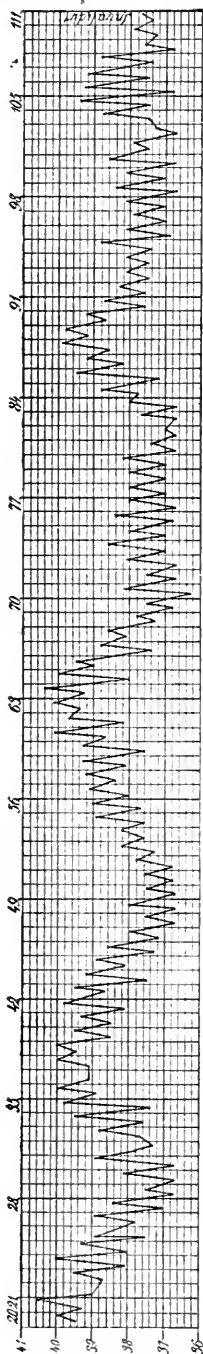
able rise of temperature sets in (43°, 44° and higher) and may be main-
tained even after death.   In other cases the fatal termination may be the
consequence of complications such as pneumonia, endocarditis, or exces-
sive anæmia.   MacLeod communicates a case in which, early in conva-
lescence, purpura hæmorrhagica sets in (cutaneous hæmorrhages, bleeding
from the nose, mouth and urinary bladder) and death rapidly ensued.

Hughes distinguishes three *types of the disease :—*
(1) The *undulant*, which is characterised by the undulations of temperature as
described.
(2) The *malignant*, in which a typhoid state rapidly develops, death occurring usually
between the fifth and twenty-first days through hyperpyrexia, cardiac weakness, or
lobular pneumonia.   Sometimes the malignancy only develops during the later stages
of cases that were mild at the commencement.
(3) The *intermittent*, which is distinguished by an intermittent fever maintained for
months with less pronounced undulations.   The duration of this type is generally shorter
than the undulating type and the complications are milder.
These types are not distinctly divided the one from the other, but run into each
other, and besides these there are irregular and mixed types.

The *percentage of mortality* is given by Hughes as a little over 2 per
cent.   In Malta the illness has gradually diminished during the last
decades.   During the sixties it still averaged 3·08 per cent., in the
seventies 2·6 per cent., and in the eighties only 0·93 per cent.

PATHOLOGICAL ANATOMY.

The principal changes found in persons dead of Mediterranean fever
concern chiefly the *intestine* and the *spleen*.

The mucous membrane of the *intestine* is hyperæmic, sometimes along
the whole course, sometimes only in parts.   The solitary follicles and
Peyer's patches are mostly unchanged ; a few of the latter in rare cases
are swollen.   Ulcers, as a rule, are not present.   Hughes only found
ulceration in three cases out of sixty-two.   In case 1 the ulcers were
situated in the cæcum and colon, a mesenteric gland having suppurated ;
in case 2, four ulcers were found in the ileum, of which three corresponded
to Peyer's patches ; in case 3, one was found in the rectum.   Hughes
regards the presence of these as accidental and as having no direct specific
connection with the illness.

The *mesenteric glands* were sometimes found to be enlarged.

The *spleen* is enlarged, hyperæmic, and occasionally soft and deli-
quescent, in some cases, however, of normal consistency.   The Malpighian
bodies are enlarged.

The *liver* is frequently enlarged likewise and is hyperæmic ; the gall
bladder distended with thick bile.   Under the microscope slight swelling
of the hepatic cells is found, and the interlobular tissue is infiltrated with
small round cells (Bruce).

The *kidneys* are hyperæmic and exhibit glomerulo-nephritis (Bruce).

The *lungs* always appear very congested and are sometimes pneu-
monically infiltrated ; the mucous membrane of the bronchial tubes is
almost always injected.

DIAGNOSIS.

The diagnosis of Mediterranean fever is not always easy, the differen-
tiation between Mediterranean fever and typhoid occasionally presenting
some difficulty.   The long duration, the appearance of relapses, the pro-

fuse secretion of sweat, the occurrence of articular affections, neuralgia, epididymitis and orchitis, and the milder course of the disease, proclaim it to be Malta fever. Cases, however, do occasionally occur in which the diagnosis is only established at the autopsy.

Confusion of Mediterranean fever with relapsing fever should hardly be possible. The sudden rise and as sudden fall of temperature in the separate attacks, the shorter duration, and the smaller number of attacks (mostly only two or three), the absence of articular affections, neuralgia, &c., and above all the presence of spirilla in the blood, should be sufficient to differentiate relapsing fever from Mediterranean fever.

Wright was the first to recommend the *serum reaction* with cultures of the micrococcus melitensis for the diagnosis of Mediterranean fever and the differential diagnosis between it and typhoid and other fevers. Monkeys gave a positive reaction as early as the day after the inoculation with the micrococcus, and this was maintained up to three years after recovery from Mediterranean fever. Of nine persons examined who had had the illness five years previously, a negative reaction obtained. This observation was confirmed by Kretz, Aldridge and others. The earliest term at which the reaction was found was the fourth or fifth day. The serum diagnosis can also be established with dead cultures. The technique of the same is minutely described by Hughes in his "Monograph," p. 158.

PROGNOSIS.

The prognosis, as a rule, is favourable.

PROPHYLAXIS.

General prophylaxis is afforded by living under favourable hygienic conditions, especially healthy dwellings. *Personal prophylaxis* demands the avoidance of the usual well-known incidental causes.

TREATMENT.

The method of treating Mediterranean fever is purely empiric.

The *fever* is most successfully combated by cold spongings, wet packs or baths, used in the same way as in typhoid.

For the *pains in the head, limbs* and *loins*, and for the *neuralgia*, antipyrin and, if necessary, morphia, are recommended, while the *sleeplessness* is relieved by antipyrin, or chloral hydrate with bromide of potassium.

The *vomiting* is usually checked by small pieces of ice and by morphia.

For *constipation*, enemata and mild aperients, especially castor oil and calomel, should be administered. To check the diarrhœa when the usual astringents have proved ineffective, more especially if there is a tendency to hæmorrhage, Notter advises the use of ferri perchloridum.

The affected *joints* should be suitably bandaged in cotton wool or flannel, and inunction of liniments or painting with tincture of iodine may be useful. Hughes recommended salicylate of quinine.

When *epididymitis* and orchitis are present, elevation of the part and the application of poultices are indicated.

Cardiac weakness demands the administration of stimulants and of digitalis.

The *nourishment* of the sufferers requires great care. At first liquid

foods must be given to them (milk, bouillon, gruel, broth thickened with barley and with the addition of egg, &c.), and only after the fever and diarrhœa have subsided may more solid food be gradually adopted.

During *convalescence* the patient should be given strengthening food, wine, quinine, iron. Complete recovery seldom occurs without *change of climate*.

When sent home most patients rapidly recover their former strength, but the voyage home must not be undertaken too early, only when convalescence has begun. Patients, however, should, as soon as possible, be removed from the unhealthy neighbourhood in which they fell ill.

As to the *serum therapy* of Mediterranean fever, but few results have as yet been published. Aldridge made use of it in five cases, of which there were results in two, no results in two, and only evanescent results in the fifth. Fitzgerald and Ewart cured an obstinate case with serum injection, but after the injections the patient had severe urticaria with high fever. Fitzgerald and Ewart, however, state that about fifty cases had been thus treated at Netley with favourable results.

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V.

INDIAN NASHA FEVER.

At the Indian Medical Congress of December, 1894, Fernandez[1] reported a disease occurring in *India*, more particularly in Bengal. It is an acute febrile infectious illness, known there by the name of *nasha fever;* in the North Western Provinces it is called *nakra fever*, and elsewhere the disease is designated *nakra jawhur*.

According to Fernandez's description, this illness is characterised by a severe *attack* of fever lasting several days, initiated by a rigor, and generally preceded by a peculiar *hyperæmia* of the nasal *mucous membrane*. The latter may be red and swollen on one side or both, there is, however, never any secretion of a muco-purulent nature, and very often also no pain. Fernandez regards this affection of the nasal mucous membrane as a local manifestation of slight cerebral hyperæmia.

The fever is mostly remittent, occasionally intermittent, and is accompanied by the usual symptoms of fever. Constipation and nausea are particularly marked. The patients complain of heat, a fulness in the head, and severe frontal headache ; they likewise complain of severe pains in the nape of the neck, the shoulders and the loins. The pains in the neck are at times so pronounced that they simulate the pains of tubercular meningitis. The face is reddened and the pupils contracted. Occasionally the fever is accompanied by an exanthem consisting of small pinkish-red spots, and which seem to occur synchronously with bronchial symptoms. As to the remaining objective symptoms which the patients exhibit Fernandez gives no account, and does not mention if there is enlargement of the spleen or not.

The fever lasts from three to five days, the swelling of the nasal mucous membrane disappearing simultaneously with the fever. Occasionally the swelling of the mucous membrane suddenly vanishes, when serious symptoms set in ; the fever increases, delirium and coma supervene, and death may ensue. Such a termination, however, is of rare occurrence.

Frequently such attacks are repeated at intervals of a month, a fortnight, or a week, when a hypertrophy of the mucous membrane of the nose is apt to develop.

The *etiology* and nature of this illness are obscure. Opinions as to the relation of nasha fever to malaria are, according to Fernandez, divided. The illness certainly rages in malarial districts, but quinine is quite

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[1] Nasha fever, the Indian Medical Congress, December 24-29, 1894, *Lancet*, 1895, January 5, p. 69.

inefficacious. We have not been informed if it be contagious or not. Crombie, as a matter of fact, doubts its specific nature.

The seasons exercise a decided influence on the frequency of the disease. The majority of attacks occur between April and August.

The Hindus in Bengal are more subject to the illness than the Mohammedans; Europeans appear not to be attacked by it. Persons under 13 or 14 years of age, and over 50, appear exempt, and persons whose occupation exposes them to the deleterious influences of the weather, such as fishermen, washermen, gardeners, &c., are particularly predisposed to the illness. The following seem to exercise a predisposing influence :—eating stale previously cooked rice with cold water, a custom prevalent amongst the poorer population of Bengal, drinking the milk of young cocoa nuts, eating portions of very young palms, and all other weakening causes.

As to the treatment, Fernandez recommends first, the administration of a strong saline aperient followed by a diaphoretic ; the nose should be sprayed two or three times daily with cold or iced water. Pain is successfully combated by opium. Locally, bleeding by punctures made in the nasal mucous membrane, or the use of astringents, such as tannin, and nitrate of silver and cocaine (10 per cent.), have given favourable results. Antipyretics are useless.

VI.

JAPANESE RIVER OR FLOOD-FEVER

DEFINITION.

Bälz (in conjunction with Kawakami) has, under the name of *Japanese River or Flood-fever*, described an acute infectious disease with a typical febrile course. This illness, to which Bälz first directed attention in 1879, is peculiar to Japan, and occurs endemically in narrowly defined districts subject to regular floods. It commences with circumscribed cutaneous necrosis, which may be accompanied by swelling of the lymphatic glands with an exanthem on the skin.

The natives call this disease *Shima* mushi, *i.e.*, island insect. It was also first described by Palm (1878) under this designation.

GEOGRAPHICAL DISTRIBUTION.

The geographical region of the distribution of river fever is, according to our present knowledge, a remarkably small one. According to Tanaka it is confined *to the banks of several rivers on the west coast of the principal island of Japan, which at regular seasons overflow*. Such are the Omonogawa and Minasegawa in the Akita-Ken (Ken signifies district) and the Shinanogawa, Akagawa, Uwonumagawa and Hajadegawa in the Nügata-Ken. Even on the banks of these rivers the disease does not occur along the whole extent of the flooded district, but only in certain places, and is completely unknown in the vicinity of other rivers which are equally subject to yearly floods.

There are no accounts of this illness from other countries.

SYMPTOMATOLOGY.

There are hardly any *prodroma* in river fever. Should such occur, however, they consist in uncertain disorders of the general health, low spirits, giddiness, disinclination to work and bad appetite.

General feverish symptoms precede the *actual outbreak* of the illness by two or three days. The illness is ushered in by repeated fairly severe rigors. These are accompanied by violent headaches always localised in the temples and forehead, palpitation in the temples, loss of appetite, abnormal sensitiveness to draughts or wind, and also a sensation of weakness that impels the patient to lie down.

On the first or second day of the disease *pain in the lymphatic glands* of one part of the body sets in, it may be in the groin, the axilla, the neck, &c. The pain causes search to be made at the seat of the part affected, when, without exception, a small round, more or less black, dry scab is discovered, which in all probability had developed during the period of incubation. Soft, warm, somewhat moist parts of the skin, particularly the genitals and their vicinity, the axillæ and the hypochondria, are the spots of predilection of these *circumscribed necroses of the skin*. The scab, which is from 2 to 4 mm. in diameter, is very hard and tough, and at first clings very tightly. Its periphery, which is but slightly, if at all, injected, is soft, dull-red and not tender either to feeling or on pressure. Sometimes, according to Bälz, there are two, three, or even four such necrotic spots, an observation on which Tanaka throws doubts. No thickening of the lymphatics can be felt along the parts between these spots and the lymph glands, but such parts are often painful on pressure.

The lymphatic glands are enlarged but not very hard, they are movable and very sensitive to pressure. The swelling and pain are not confined to these glands, but in a less degree attack all superficial glands, mostly symmetrically. For instance, if the seat of the necrosis is on the right side of the scrotum, the left inguinal glands, as well as those on the right side, will be affected.

The *temperature* during the first days fluctuates between 38·5° and 39·5°. The *pulse* at the same time is relatively but little accelerated, being in men about 80, and in women 100 per minute or more.

Conjunctivitis is almost always present. The palpebral conjunctiva in particular is much reddened, and in the mornings the eyelids are mostly stuck together. At the same time the whole eyeball appears to be swollen, prominent and staring.

The nose and throat are almost always normal, yet a cough and rhonchi can be heard over the lungs. The first cardiac sound is frequently impure.

The tongue is moist and but slightly coated. There is generally rather obstinate constipation. The *spleen* is always *enlarged*, but not to a great degree; the *urine* is diminished and frequently contains albumen (Tanaka). Often, also, stranguary is observed.

The fever increases during the following days, and by the evening of the fifth or sixth day has attained 40° or more. The fever, as a rule, is continuous, more rarely remittent. The pulse frequency at the same time is relatively slow.

On the sixth or seventh day an *exanthem*, accompanied by a still further rise of temperature, breaks out ; this first appears on the face and on the temples and cheeks. The exanthem consists of large, irregular, dark red papules, which are often confluent on the cheeks. The eruption spreads to the fore arms, legs and trunk, whereas it is indistinct on the thighs and upper arms. The throat and palate generally remain free, exceptionally a few punctiform spots are observed on the latter. Simultaneously with the papules, and between these, there appear on the fore arms and the trunk exceedingly numerous, small, dark red nodules, in the centre of which frequently a little hair is visible. The exanthem, which varies in distinctness and does not itch, is of uncertain duration, on an average lasting from four to seven days, and in mild cases occasionally only a day.

The duration of the exanthem indicates the *maximum of the complaint*. The fever is continuous. The temperature rises to 40°, 40·5°, or even (but very rarely) to 41°, while the frequency of the pulse fluctuates between 80 and 100. The pulse is full, never dicrotic.

The patients look flushed and feverish, and are often delirious at night, but always give clear answers to questions. They complain a great deal during the whole of the illness. Bälz attributes this to general hyper-æsthesia; in severe cases the muscles are sensitive on pressure. There is frequently hardness of hearing, presumably of a nervous character, and which is apt to continue during convalescence. The lips are dry, fissured, and easily bleed. The tongue in serious cases appears dry and coated at the edges and smooth in the centre, as if polished. It can only be moved with difficulty. The gums are in a condition resembling that met with in scurvy. In serious cases the epigastrium and the left hypochondrium are somewhat sensitive on pressure. The stool is constipated throughout the illness, the spleen somewhat enlarged. The cough is sometimes very violent, coming on in paroxysms, and is harsh and hoarse; the respiration, especially in women and children, is much accelerated. In the meantime the scab has usually fallen off, and in its place there is a crater-like ulcer with sharp steep edges and which exudes only a little pus. The patients perspire freely, and in consequence sometimes exhibit extensive sudamina.

About the end of the second week—in mild cases before, in serious cases later—a marked *remission of fever* occurs, and the temperature returns to normal in the course of a few days; meanwhile there is an improvement in the condition generally. The patient recovers appetite, and frequently there is slight diarrhœa; the urine becomes more copious, and deposit of urates is the rule. The patients generally recover quickly, but the ulcer may take weeks to heal, and the sensitiveness of the glands in its vicinity continues even when convalescence is far advanced; the other glands affected become normal before the fall of temperature.

This is the course of disease in what we may term typical cases. Besides these, still milder and more severe forms occur. In the *milder* cases the general symptoms remain in the background, the fever may be so slight that patients are not obliged to keep their bed, the exanthem is trifling or entirely absent, the cutaneous necrosis and glandular enlargements are, however, always present. The extent of the local affection is in no way proportionate to the degree of the general condition. The largest ulcer ever observed by Bälz was on the person of an ambulatory case of the disease.

In the most *serious forms* it is more often the complications than the hyperpyrexia that endanger the patient's life and cause death. Such complications are parotitis; copious, sanguineous, tarry stools; serious nervous symptoms arising during convalescence (coma, mania); cardiac weakness and œdema of the lungs.

The average *duration* of river fever is, in moderately severe cases, three weeks, it is quite exceptional for the disease to last a month. Mild cases sometimes only last a week.

The mortality is given by Bälz as 15 per cent., while according to Tanaka it may be 40 per cent., or even 70 per cent. or more.

PATHOLOGICAL ANATOMY.

The pathological material hitherto available is principally limited to two *post-mortem* examinations undertaken by Kawakami. The result of these autopsies was that *distinct local lesions are not to be found anywhere*.

The lungs exhibited hypostases, the bronchial mucous membranes were much

swollen and reddened, the myocardium appeared soft and easily compressible (both cases had been drunkards), the spleen was enlarged and slight perisplenitis was present. The small intestine in the vicinity of the cæcal valve appeared here and there to be much injected and showed somewhat raised areas, which did not always correspond to Peyer's patches. The mesenteric glands were somewhat swollen, the peritoneum covering the stomach, the liver and the omentum was injected.

ETIOLOGY.

River fever is an *infectious disease.* The unknown virus of disease, according to Bälz, clings to the submerged soil of the above mentioned valleys, which are annually flooded; the floods doubtless playing an important part in the development of the virus of disease. The floods occur regularly during the spring and summer. Hemp or corn is sowed on the strips of river bank that have been flooded, and during the harvest in July and August the illness sets in. The reapers who are at work all day in the fields are almost exclusively attacked ; it is but rarely that other workers, who pursue their calling in the immediate vicinity of the river, are taken ill. Occasionally, however, persons fall ill who have never been on the soil, or even come into contact with the harvested hemp or corn. From this fact one must conclude that the virus of this disease may be carried by the corn or hemp or other articles, possibly also by particles of soil clinging to such articles, the illness becoming thereby, though only *in a limited degree,* transportable.

The affection is *not contagious.* No transmission from one member of a family to another takes place.

That part of the skin on which the circumscribed necrosis appears is probably the spot where the virus of disease has penetrated the body. As Bälz mentions, the scab is generally situated on parts of the skin which by reason of their natural moisture, and the more or less viscid and sticky character of their secretions, are particularly adapted to retain the smallest atoms rising with the air.

Bälz has convincingly contradicted the assertion of Japanese doctors that the illness is originated by a species of acarus related to the leptus autumnalis, which bores into the skin. It is called by the Japanese *akamushi, i.e.,* the red insect or *kedani, i.e.,* the hair louse. There is, however, no proof that the bites of such insects, the same as other slight injuries to the skin, may not form the point of entrance of the virus of disease. Takana, at three autopsies, found a species of proteus partly mingled with staphylo- and strepto-cocci in the lungs, and was even able to confirm the presence of these in the urinary sediment and sputum of the patients. Takana, therefore, regards this micro-organism as the cause of the illness.

The *period of incubation* averages four to seven days.

Neither *age* nor *sex* exercises any predisposing influence. Though men fall ill more frequently than women or children, the cause is that the former are more exposed to the infection.

Pregnant women who contract the disease often miscarry and their illness mostly has a fatal termination.

The predisposition to the illness is not extinguished by having previously had the disease. *Several attacks* in the same person have been observed, but subsequent illnesses are milder than the first one.

PROPHYLAXIS.

Bälz, in order to ensure the sanitation of the soil in places subject to the illness, recommends that it be speedily cultivated with plants which experience has proved to have a salutary influence on bad land, and for

this purpose suggests, above all others, the planting of the eucalyptus globulus and of the Japanese Kiritree (Paulownia imperialis).

If Bälz's opinion as to the invasion of the virus of disease into the body is correct, those persons who are compelled to expose themselves to the infection should protect themselves by scrupulous cleanliness, a goal easily attainable by frequent baths and thorough washing.

TREATMENT.

The *treatment* of river fever is symptomatic.

High *fever* requires the administration of *antipyretics* (phenacetin, antipyrin, quinine, sodium salicylate). Cool or cold baths are not well borne by the Japanese. Even antipyretics must be carefully given, for, according to my experience[1] of the treatment of typhoid, which coincides with Bälz's, the Japanese react to these drugs more strongly than Europeans; 1·0 quinine, or even 2·0—3·0 sodium salicylate sufficed to bring the temperature down several degrees. Larger doses induce danger from collapse. Even after the administration of such moderate doses as those mentioned, I have repeatedly observed a fall of temperature of 5° or even more.

The *sleeplessness* and annoying cough are combated by narcotics; constipation by alteratives or enemata.

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[1] *Klinische Beobachtungen über die Krankheiten Japans. Virch. Archiv.*, xcix., 1885 p. 368.

VII.

THE MALARIA OF WARM COUNTRIES.

DEFINITION.

UNDER the term *malaria* (from mal' aria, Italian for bad air) is comprised a group of ailments occurring endemically and epidemically, and which, notwithstanding the great diversity of the manifestations of the disease, exhibit in regard to their etiology, symptomatology and therapeutics, an undeniable homogeneity. Malarial fevers are all attributable to certain blood parasites, and are distinguished by a great tendency to periodicity. Quinine is the most effective prophylactic and remedial agent. Europeans in the tropics suffer severely from malaria in one or other form, and the presence or absence of malaria in a place, is decisive as to whether the climate is unhealthy or not. This disease, therefore lays claim to our most particular attention.

SYNONYMS.

Wechselfieber, Intermittens, Cold fever, Marsh fever, Paludism, Swamp fever, Climatic fever, Malarial diseases, Ague, Intermittent fever, Paludal fever, Jungle fever, Hill fever, Mountain fever, Coast fever, Gnat fever (Ross), Hæmamœbiasis (Ross), Maladies Palustres, Fièvre Paludienne, Paludisme, Febbre intermittente; Koorts.
The disease, also, is often called after places, as: Dacia, Batavia, Cameroon fever, &c.

HISTORY.

The history of malaria, and more particularly of those forms peculiar to warm countries, and which formerly had a far greater distribution than they have at the present time, may be traced back to the most ancient times. According to W. Groff, malaria was known to the ancient Egyptians. The word "*Aat*," which, amongst others, occurs on the inscriptions of the temple at Denderah, is supposed to indicate the annual recurrence of the disease. Hippocrates (460-377 B.C.), divided the fevers "without distinct pains," that is to say, without perceptible manifestations, which he observed in Greece, into continued fever, daily fever, tertian fever and quartan fever. Even malarial cachexia was known to him; he descants on splenic disease and dropsy in connection with fever. Celsus (first century, A.D.) describes the various forms of ague and mentions a condition which is identical with malignant tertian fever. The more minute study of malarial diseases, however, only commenced after the introduction of cinchona bark from Peru into Spain by the Viceroy Del Cinchon and his physician-in-ordinary, Juan del Vego, in 1640; the latter being competent, by the administration of the bark, to distinguish malaria from other fevers. In 1712, Torti's

epoch-marking work (Therapeutica specialis ad febres quasdam perniciosas) appeared, and in which the first classical description of pernicious malarial fevers was given. Afterwards, in 1716, Lancisi's investigations on the etiology of malaria (De noxiis paludum effluviis eorumque remediis), were published. The extensive colonial settlements of the eighteenth century showed the great distribution of malarial disease over the surface of the globe. Andouard was the first who, in several works appearing between 1803 and 1823, called attention to the constant enlargement of the spleen. Further landmarks in the history of malaria are pointed out by the discovery of melanæmia by Merckel, Virchow and Heschl (1847-1850), and the discovery of the malarial parasites by Laveran (1880). Since then study has been particularly directed to the parasites, and it is to the Italian investigators in the first place that the credit is due of having elucidated the etiology of malaria. For the late discoveries of the mosquito theory and the development and demonstration of its correctness, our thanks are due to Manson and Ross.

GEOGRAPHICAL DISTRIBUTION.

(COMPARE CHART I.)

The geographical region of distribution of malarial disease is extraordinarily large. In this respect no other infectious disease can compare with it. In the eastern hemisphere, 63-64° N. lat. (Sweden, Finland) forms the western boundary, and 55° N. lat. (Northern Asia) the eastern boundary.

In the western hemisphere, 55° forms the western limit at which malaria occurs and 45° the northern limit ; the southern limit in America is 35°, in Africa 30°, and in Australia 20°, S. lat.

Malaria prevails *in the most temperate and also in the torrid zone, but as the Equator is approached it increases in extent and intensity.* With the exception of the waterless deserts (Sahara, Arabia, Atacama and Central Australia) there is no extensive continental region on or near the shore that is free of malaria, whereas some of the tropical islands are exempt.

I will therefore confine myself to the mention of the *most important* malarial districts.

In EUROPE these comprise the North German low-lying plains, especially the Baltic coast of Prussia, Pomerania, and Mecklenburg, Northern Silesia, the river plains of the Mark, the swampy and pasturage lands of Hanover and Oldenburg, the Western coast line of Schleswig and Holstein, the lowlands of Westphalia, along the Rhine and its tributaries, in Holland and the low-lying districts of Belgium ; in France, the West Coast, the bed of the lower Loire, the Sologne in department Loir-et-Cher, the Brenne in department Indre, the delta and banks of the Rhone, and the marshy Dombes between the Saône and the Ain ; in the Spanish Peninsula, the valleys of the Guadalquiver, Guadiana, Tajo, &c. ; the Balearic Islands ; in Italy, the valley of the Po and its tributaries, the extensive West Coast which extends from the mouth of the Arno, through the Maremmas of Tuscany, the Roman Campagna, the Pontine marshes, and the West Coast of Naples as far as Calabria; also in Sicily, Sardinia and Corsica, Dalmatia and Istria; in Turkey, at many places along the lower regions of the Danube ; the Hungarian valley; the coasts of the Black Sea, the Sea of Azov, and the Caspian Sea, including the adjacent steppes; in Russia the valleys of the Dniester, the Dnieper and the Volga ; the Caucasus ; in Sweden, principally on the shores of the large lakes in the south ; in Denmark only in the Islands of Laaland and Falster ; and perhaps the East Coast of England.

In ASIA malaria is endemic on the coasts of Asia Minor and Syria;

in the valleys of the Euphrates and Tigris; on the Coast of the Persian Gulf; on the lofty plain of Teheran (mountain fever); on the shores of the Caspian Sea, on the great steppes; in the valleys of the Indus, Ganges and Brahmapootra, which periodically overflow their banks; in India where the plains join the hills at the foot of the Nilgiris, the dry, grassy Highlands of the Deccan, and the jungle of Terai at the foot of the Himalayas are reckoned the most dangerous districts; in Ceylon; in Further India (Singapore is relatively immune); in the Indian Archipelago, more especially on the Nicobars, Sumatra, Java, where the harbours of Batavia, Tandjong Priok are particularly dreaded; in Borneo, Amboina, on the Coasts of New Guinea; in the Philippines; in the tropical and subtropical parts of China; in Corea; and in Japan, where malaria is frequent in the swampy rice fields, but is generally benign.

In AFRICA the most notorious malarial centres are the river beds of the Senegal and Gambia, the Guinea Coast from Sierra Leone to Cape Lopez, the basin of the Congo, the east coast upwards from Delagoa Bay, including the entire hinterland, and more especially the vicinity of the great lakes, Massowa, the swampy valleys, plains and shores of the lakes of Abyssinia; the entire district which extends from the western declivities of the highlands of Abyssinia over Nubia, Kordofan, and Darfur, to Lake Tchad; a few districts in the delta of the Nile, especially near the great lakes (the remainder of Egypt is free of fever), Tripoli, Tunis, Algiers, many oases of the Great Desert; of the African Islands, the islands of Cape Verdi, the Comores, Nossi-Bé, Madagascar, Réunion and Sokotra, and also Mauritius, where malaria has only during the last decade appeared in a malignant form. The Seychelles, St. Helena; the island Rodriguez, though contiguous to Mauritius and exposed to the same climatic influences, and the Cape, enjoy almost absolute immunity. The same holds good for the Australian Continent and Tasmania, as well as most of the Polynesian islands; malaria is totally unknown in the Fiji Islands; but it rages in a malignant form on the New Hebrides.

In AMERICA the geographical region of distribution of the disease includes the southern, central and prairie states of the United States of North America, the coasts of the Gulf of Mexico and of the Caribbean Sea, the West Indian Archipelago; a few islands, Barbadoes in particular, enjoy relative immunity; Venezuela, Guiana, northern Brazil, Paraguay, Bolivia, and the northern part of the Pacific Coast of South America.

In all these countries malaria is endemic. From time to time, however, and generally palpably induced by meteorological influences, such as excessive falls of rain, floods, great heat or drought, or the sudden sinking of standing surface water, *epidemics* occur which are distinguished for their severity, and run a course fatal to both aliens and natives. These epidemics, moreover, may extend to regions in which malaria is not endemic. Outbreaks of malaria may spread over vast tracts of land and, occasionally covering entire continents, may cause actual *pandemics* that may last months or even years. Such a pandemic raged during 1557-1558, when nearly the whole of Europe was attacked by it. During the two following centuries and also during the nineteenth century, a series of severe epidemics came under observation, the most extensive of these occurred from 1823-27 and visited nearly all the countries on the face of the globe; the last epidemic, 1866-1872, spread over a great part of Europe, many districts of India and North America, and it was during the course of this epidemic that the two East African Islands, Mauritius and Réunion, which had hitherto enjoyed almost complete immunity, were subjected to a severe visitation of malaria.

The *epidemic occurrence* of malaria on *board ship* will be discussed later.

ETIOLOGY.

The investigations of the last twenty years have resulted in the discovery that malarial diseases are originated by *certain living organisms which cling to or invade the red blood corpuscles and which belong to the order of the protozoa*.

The malaria parasites were, in 1880, discovered by Laveran in Algiers. At first this discovery was repudiated, then it was confirmed and considerably amplified, especially in Italy, by Marchiafava, Celli, Golgi, Bignami, and others. The etiological importance of the malaria parasites is now universally acknowledged, and it has been proved that they appear with great regularity—to practised investigators almost constantly—in the various forms of malaria, and that their period of propagation coincides with the attack of fever. The malaria parasites are never found in other diseases unless complicated by malaria.

Further confirmation of the opinion that these blood parasites are the cause of malaria is furnished by the experimental investigations which were first undertaken by Gerhardt in 1884, and later were mostly conducted in Italy. The experimenters succeeded, by means of injecting the blood of malarial patients subcutaneously, or into the veins of healthy persons, in generating malaria, which in most cases was of the same type of fever as that from which the original patient was suffering; this was especially the case in the carefully observed experiments of 'Di Mattei.

The separate types of malaria are caused by separate parasites, which are distinguished by differences in their growth and pigmentation, and more particularly by the diverse duration of their development. Opinions are divided as to whether it is the question of the same or different species, or of morphological varieties of one and the same kind. Laveran retains his opinion of a polymorphous parasite, and his conviction as to the specific nature of malaria organisms is supported by Babes, Georghui, Kanellis, Cardamatis, and A. Plehn. It is not unreasonable to suppose that, under different conditions of climate, seasons, and soil, or under the influence of their animal host, namely, the organic fluids of man, different modifications in the form and virulence of malaria parasites may occur.

The fact, also, that in epidemics of malaria all forms of the disease occur, lends still more colour to Laveran's opinion, while the results of experimental inoculatory transmissions, favour the views of those who maintain the idea of different species.

The following types are distinguished : (1) The *quartan parasite* (Golgi), which accomplishes its development in three days and is the cause of quartan fever (see fig. 13, table II). In its early stage the parasite appears as a small transparent unpigmented form, with indolent, amœbic movements. It invades a red blood corpuscle, gradually increasing in size, while the amœbic movements decrease, but a gradually increasing formation of black, brown, or lighter-hued granules of pigment are seen merrily darting to and fro within the body ; the blood corpuscle meanwhile, grows paler and paler. Finally the parasite, resembling a round disc, entirely fills and well nigh obscures the corpuscle. The pigment now assumes a central and radiated position, and a spoke-like design now first appears on the disc, which later on shows a

radiated division into from six to twelve pear-shaped segments (*daisy or rosette form*).   At last the whole break up into the same number of small, roundish little bodies—erroneously called spores—which, like the pigment, become free.   This separation occurs simultaneously with the commencement of the fever, or shortly precedes it.   The spores, which represent a new generation, again seek red blood corpuscles, and thus the process commences anew.   Sometimes two, or even three, parasites invade one blood corpuscle.   The released pigment is taken up by leucocytes and deposited in the vessels of certain organs with weak flow of blood, especially the spleen, liver, and bone marrow.

(2) The *tertian parasite* (Golgi), the cause of tertian fever, requires two days in which to accomplish its development (see fig. 14, table II.).   The adolescent form has more mobility than the quartan parasite ; it develops in the red blood-corpuscle, which becomes discoloured and attains dimensions double its normal size.   The parasite has the appearance of a sphere which, after the collection of the pigment in its centre, falls into 15-20 spores that are smaller than those of the quartan parasite, and form an irregular little heap, reminding one of a bunch of grapes or mulberries ; more rarely they form two circular rows (*sunflower shape*).

Through the presence of two or three broods of quartan or tertian parasites of different ages, developing at intervals of twenty-four hours, those types of fever designated double quartan, triple quartan and double tertian, are originated ; the two latter being sometimes named quotidian fever.   Through irregularities in the duration of development of the parasites irregular fevers are caused.

(3) *The parasites of malignant tertian fever* appears in Italy in summer and autumn in contradistinction to the benign tertian fever of spring (Marchiafava and Bignami), and is identical with *tropical malaria* (see fig. 5).
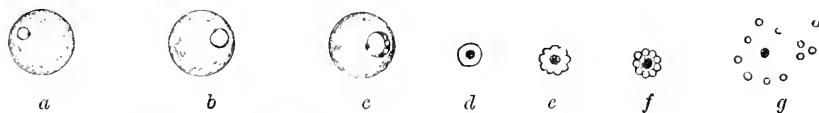
FIG. 15.—*The parasite of tropical* malaria, after R. Koch.   *a*, Red blood corpuscle with small annular parasites ; *b*, red blood corpuscles with medium-sized annular parasites ; *c*, red blood corpuscles with large ring-shaped parasites ; *d*, circular parasite with an agglomeration of pigment in the centre ; *e*, lobulated parasite ; *f*, rosette-form arrangement of the spores ; *g*, free spores with residue in the centre ; *d-g*, from the spleen of a cadaver.

The cycle of development lasts forty-eight hours.   The parasite is a small, briskly moving little body, smaller than the former two.   In a condition of rest it assumes the so-called ring or signet-ring form or, more correctly speaking, the form of a disc with a ring-shaped stained outline. Its minimum size is, according to R. Koch, $\frac{1}{8}$ or $\frac{1}{6}$ the diameter of a red blood corpuscle.   When it has attained its greatest circumference, its size is about $\frac{1}{3}$ of that of its host.   In stained preparations the circlet of the small and medium sized parasite is seen to consist of a thin circular line which exhibits at one, or occasionally at two, opposite places a dark spot. It is only when the parasite has almost attained its full dimensions that the half of the circular line opposite to the dark spot becomes broader and assumes the shape of the crescent moon.   In this gaps are often seen which perhaps represent vacuoles.   The parasite at first appears colourless, but is only seemingly unpigmented.   It contains the pigment in

such remarkably tiny particles, that it is only with particular attention that the pigment may be observed in the large parasites, at the broad portion of the crescent, as a brownish gleam. The stronger or weaker pigmentation also depends on the preparations; in fresh preparations the parasites appear more pigmented than in stained preparations, the pigment being partly removed by the alcohol and partly concealed by the dye. In dead parasites taken from the cadaver, the pigment is found rolled up in a lump (Koch). After finishing its growth the parasite forms spores. It becomes lobulated, rosette-shaped, while the pigment collects at the centre or more towards the periphery, and is finally divided into six to twelve little balls. The propagation, however, rarely takes place in the peripheral blood, more generally occurring in internal organs, particularly in the spleen, bone marrow and the cerebral capillaries. The parasites disappear out of the blood, so that during the attack generally only a few are found, and sometimes none at all. Whereas in ordinary tertian fever the infected red blood corpuscles swell up, in malignant tertian fever they tend to shrivel and become darker, assuming a tint reminding one of old brass.

(4) *The crescents or sickle forms of Laveran* (see fig. 18, table I.). These are oval, fusiform, or crescent-shaped formations, pigmented in the centre, which have *no amœboid mobility*, but possess the capacity of slowly altering their shape (Mannaberg). When completely developed, their size exceeds that of the red blood corpuscles. They are found partly in red blood corpuscles, or clinging to the same, partly free in the blood, sometimes also contained in leucocytes. They are found in severe *forms of malaria*, originated by the malignant tertian parasites, but not in the benign quartan and tertian fevers; nevertheless, like the spherical and flagellated forms mentioned below, they have no relation to the fever. As a rule they only appear in the blood after the fever has been present some time, and are still met with long after the patient has recovered from the effects of malaria. They are probably, originally, malignant tertian parasites that have failed to sporulate (according to Mannaberg they consist of two parasites that have invaded the same blood corpuscle and coalesced, he therefore calls them syzygi) and represent sterile forms, which, however, as we shall presently see, are of great importance to the further fate of the parasites.

As they may be seen by means of Romanowsky's process of staining (see p. 104) they contain chromatin.

Inoculatory experiments undertaken by Elting with blood that only contained the crescents and oval forms of æstivo-autumnal parasites gave negative results.

In Cameroon F. and A. Plehn very rarely found crescents (at most in one case out of ten).

(5) *Flagellated bodies.* [Corpora flagellata, polymitus form[1]] (see fig. 16, table II.) These are spherical pigmented little bodies, about the size of a red blood corpuscle, that are free in the blood, and that are provided with one to four long, delicate, mobile flagellæ that sometimes terminate with a slight enlargement. It is observable by the microscope how the flagellæ when thrown off dart through the plasma with lively snake-like movements.

The flagellated bodies are present in *all forms of malaria*. They are, however, not seen in the blood immediately after its removal from the blood-vessels, but only after some minutes, usually not before a quarter of an hour (Manson). They originate from the large, free, pigmented spheres that are merely parasites that have not sporulated (as occurs in

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[1] From πολύμιτος, *i.e.*, many threads.

all kinds of parasites), or from crescents—these previously assuming first an oval, then a spherical form—by the shooting out of processes. The flagellæ that become free, and which contain chromatin, represent that form of malaria parasite that is destined to *propagate the species outside the human body.*

Marchiafava and Bignami describe a *quotidian* parasite, the cycle of whose development takes twenty-four hours, as still another kind of malaria parasite, and Mannaberg even distinguishes a *pigmented* and an *unpigmented* form of the same. It is, however, most probably identical with the parasites of malignant tertian fever, the period of development of the latter being between twenty-four and forty-eight hours, the course of development of malaria parasites being sometimes quicker, sometimes slower. The Italians likewise described a distinct difference in the sporulation of the quartan and tertian parasites, and the constant arrangement of the segments in the form of a bunch of grapes; but other investigators (F. Plehn, Bein, Van der Scheer, and others) were unable to find these phenomena. Van der Scheer, F. Plehn, and other authors only differentiate *two kinds* of malaria parasites : (1) the *large pigmented parasites,* which are present wherever there is malaria, and which originate the typical intermittent fever ; and (2) the *small slightly or non-pigmented crescent forms* peculiar to southern lands, which originate the serious forms of malaria, distinguished by a more irregular course of fever and the frequent appearance of complications. This distinction amply suffices for practical purposes (see figs. 17 and 18, table I.).

Sacharoff differentiates *parasites of the erythocytes* (quartan and tertian parasites) and *parasites of the hæmatoblasts* (quotidian parasites, malignant tertians, and crescents) ; the former attack the red blood corpuscles, the latter only the nucleated red blood corpuscles of the bone marrow, this being the reason why they are not often found in the circulating blood. The crescents, according to the same investigator, are nothing but the parasites of the earlier stages of the hæmatoblasts, while the other forms are originated by infection at later stages of development.

A. Plehn has lately described as *karyochromatophile granules* small forms that become visible in the red blood corpuscles by means of staining with acid alum-eosin solution of hæmatoxylin ; they are observable as deep blue dots or spots of varying size (up to $\frac{1}{3}\mu$). From six to twenty of them are generally contained in one blood corpuscle, and very frequently two or more are joined in chains (diplococci). They diminish or disappear after attacks of malarial fever, then again increase, and may be met with months and years after leaving the malarial district, and after the last attack of fever. A. Plehn considers these forms to be capable of proliferation and the *elementary forms of malarial parasites* (analogous to the elementary forms of the pyrosoma bigeminum of Texas fever, see p. 110), through whose transformation into the plasma the attack is occasioned. Plehn found this form in Cameroon not only in newly arrived Europeans, whose anæmia he attributes to these parasites, and in native and immigrant coloured folks, but also, though much more rarely, in inhabitants of the malarial region round Rome, and in Hamburg in sailors from various malarial countries. The suggestion that these granules might be regarded as the residue of the nucleus of red blood corpuscles is met by Plehn with the reply that notwithstanding the frequency of granulated blood corpuscles, nucleated corpuscles are very rarely found. The same basophile granules described by Plehn, have been found by Grawitz,[1] Litten,[2] and Cohn,[3] in anæmia of the most different kind and etiology. The granules, however, in these cases, have no relation whatever to malaria parasites, but are probably degenerations of protoplasm, which result from the chemical alteration of the blood always present in anæmia (Cohn).

The human body may be the host not only of several generations of one kind of parasite, but of several kinds simultaneously, these causing *mixed infections.* This, however, does not occur very often. Thayer, in Baltimore, only saw thirty-one malarial patients with mixed infection out of 1,618 ; the ordinary tertian parasites are most often found in conjunction with the parasites of æstivo-autumnal fever. Koch is of opinion that the different sorts reciprocally exclude each other.

As to the *further anatomy of malaria* parasites, it should be mentioned that they possess a vesicular-like nucleus with one or several nucleoli. The latter, in stained preparations, is particularly distinct in free young parasites, appearing as a round or angular formation which is coloured bright red (see p. 104) by Romanowsky's method of staining, and is surrounded by a lighter tinged area. The spores, also, are provided

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[1] *Deutsche. med. Wsch.*, 1899, No. 36, p. 585.   [2] *Ibid* , 1899, No. 44, p. 717.
[3] *Münch. med. Wsch.*, 1900, No. 6, p. 186.

with a nucleus. Sporulation, according to Italian authors (Grassi, Feletti and others) is accomplished by direct division of the nucleus, and according to Romanowsky by karyokinesis.

The malarial parasites have received different names: by Laveran they were first called *oscillaria*, later *hæmatozoon malariæ*; by E. Metschnikoff they were named *hæmatophyllum malariæ*, by Osler *hæmatomonas malariæ*; by Marchiafava and Celli *plasmodium malariæ*, and by Grassi and Feletti *hæmamœba*. The designation *plasmodium malariæ* has become the most popular of these. It is nevertheless a very inappropriate name, as the term plasmodium implies not a separate creature but a congeries arising from the coalescence of single-celled organisms or of single cells. This designation should therefore be again eliminated (Braun).

As to the *classification of the malaria parasites in the zoological system*, Braun considers that they belong to the class of sporozoa (appertaining to the order of protozoa) in which they, together with the analogous blood parasites of frogs, reptiles, bats, birds, form the order hæmosporidia. Feletti and Grassi assign them to the rhizopodes.

The best time for examining the blood for malarial parasites is, for the tertian and quartan parasites an hour before the attack until its crisis, for malignant tertian parasites the commencement of the afebrile period. In order to demonstrate the malarial parasites in the blood, the tip of the finger or the lobe of the ear should, after the usual antiseptic precautions, be pricked, and the blood taken should be examined either *fresh* or after being well dried in the air in the usual way, or better still by a half hour's treatment with *absolute alcohol*,[1] and stained with *methylene blue*. The blood must be spread in a very thin layer so that the blood corpuscles lie separate one from the other with their broad surface turned to the observer. In dry preparations this is accomplished by placing a cover glass, tile fashion, over one on which there is a small drop of blood, which is then allowed to spread slowly, when the two cover glasses are pulled apart. Another method is to draw the edge of the cover glass along over the drop of blood emerging from the puncture, whereby it gathers a narrow margin of blood; the cover glass is then tilted at an angle and passed over one or two others. In order to suitably preserve the fresh preparations from evaporation they are closed in with paraffin, vaseline, &c. The observation with oil immersion lenses is made with a powerful eye-piece and an Abbe's condenser. The small, unpigmented malaria parasites may very easily be confused with very similar light spots, so-called vacuoles, in normal red blood corpuscles; and spores may be confused with blood plates, or the small round atoms that become detached from the red blood corpuscles if the cover glass is slightly pressed. It is therefore advisable to *commence the study with stained preparations*.

For clinical purposes, staining with *Chenzinsky-Plehn's solution* will be found most suitable: this consists of concentrated watery solution of methylene blue 40 g., 0·5 per cent. eosin solution, in 70 per cent. alcohol, 20 g. and distilled water 40 g. This stain is permitted to take effect on the preparation by slightly warming for from thirty seconds to one minute; it is then rinsed off, dried, and examined in Canada balsam, or preferably a concentrated solution of gum arabic, as Canada balsam is too bright. The red corpuscles then assume a pink colour which, however, is less distinct in those containing parasites. The parasites, as also the protoplasm of the white blood corpuscles, appear pale blue, the nuclei of the latter are stained dark blue.

The *staining of fresh blood* also, which permits one to follow the stages of growth of the malaria parasites, is recommended. The cover glass, on which a drop of blood has been deposited, is quickly dropped on to a slide on which there is a drop of diluted methylene blue salt solution (1 drop of a 1 per cent. solution of methylene blue to 10 c.cm. of 0·65 per cent. salt solution). (Rosin.)

For the study of the more minute structure of malaria parasites, Romanowsky's method of staining, modified by Nocht, is the most appropriate; it consists of a mixture of methylene blue, red from methylene blue and eosin in a watery solution. This method is described in *Cbl. f. Bakt.*, xxv., 1889, Nos. 21-22, p. 769.

Morphologically, the youngest forms of the tertian and quartan parasites cannot be distinguished from the adult parasites of tropical malaria. The clinical condition is here of service. The large tropical parasites are found after the wane of the attack, *i.e.*, when the temperature is low; the most adolescent forms of the two other kinds are, on the contrary, found at the commencement of the attack, when the temperature is high. As a rule, also, there are found a few large parasites besides the adolescent forms of the tertian and quartan parasites (Koch).

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[1] In a tropical climate in which pure alcohol may attract a quantity of moisture from the air, F. Plehn recommends fixing for three to four minutes with concentrated alcoholic solution of sublimate, with subsequent thorough washing.

A number of preparations may have to be examined before parasites are discovered. The number of parasites as a rule increases with the severity and duration of the disease. In pernicious malaria they are remarkably numerous; Van der Scheer occasionally saw from fifty to eighty in one field of vision. On the other hand there may be severe fever, yet only a few parasites may be demonstrated in the blood from the finger. This disparity between the number of parasites and the severity of the illness is, however, accounted for when an autopsy admits of the examination of the viscera (Bignami). When infection is quite recent, as during the few first days of disease, the parasites are sometimes missed, for they are only extant in small numbers, and therefore are difficult to discover, or else they have not yet reached the circulating blood (Mannaberg.)

As to the *pathological effect of the malarial parasites*, they disintegrate the red blood corpuscles in which they have penetrated by feeding at their expense, and as products of digestion of the hæmoglobin they form pigment, melanin. It is in this way that *anæmia* and *melanæmia*, so characteristic of malaria, ensue, and in consequence of the melanæmia, melanosis of the internal organs is set up. At sporulation, a virus formed by the parasites is set free; this originates the fever and simultaneously attracts the leucocytes from the spleen, the bone marrow and the lymphatic glands into the blood, chemotaxis and leucocytosis being the result. The regular cycle of the attacks is, according to F. Plehn, explained thereby; namely, that by the chemical processes set up during the attack of fever such organisms as have not developed, as well as those that have in the meantime reached the body through fresh infection and are still in the amœboid stage, are killed.

The *debilitating disorders* and the numerous *organic diseases* which may be set up in consequence of malaria, with or without symptoms of fever, are also attributable either to the effect of the poisonous matter formed by the parasites, or to the interference with the respective organs through red blood corpuscles containing parasites, or to pigmented leucocytes. *Spontaneous recovery* takes place—as shown by the observations of Marchiafava, Celli, and Golgi—through the parasites being seized and absorbed by the leucocytes.

Schellong explains the different symptoms of malaria as occurring through capillary stasis, which ensues as a result of the disintegration of the red blood corpuscles in the various organs by the influence of the malaria parasites. Fever ensues through disorders of circulation in the heat regulating centres.

Efforts to artificially cultivate malaria parasites have hitherto failed. They have also hitherto never been discovered in inanimate objects, in the air, water or elsewhere. The statements of Coronado and Hehir, who claim in this respect to have had more success than other investigators, are not calculated to inspire confidence. Two questions are therefore raised : Whence do the malaria parasites originate ? and, by what means do they invade the human body ?

There are three hypotheses as to the mode of infection. These are :—

(1) The air theory.

(2) The drinking-water theory.

(3) The mosquito theory.

(1) *The air theory*, which is indicated by the name of the disease (mal' aria), is that the malaria parasites reach the air in some way, perhaps in atoms of dust, from the soil which contains them in some form or other, and is inhaled by the respiratory organs.

Even though, *à priori*, there is little probability that such delicate and

frail beings as malaria parasites should be able to reach the air and withstand desiccation, this theory does not coincide with the fact that frequently the malaria centre is narrowly confined. Often in one town there are healthy and unhealthy quarters. Thus, to cite a few of Bignami's examples : in Rome outside the Porta del Popula dangerous fevers occur, while the few dwellings at the commencement of the Corso, only 100 m. distant, are healthy. The hospital of S. Michele di Ripa Grande is free from malaria, but at a short distance, in the vicinity of S. Paolo, there are dangerous malarial centres. In Palo there are actually houses on the quay in the rooms of which, facing the sea, one may safely sleep, while in those facing the country one is apt to get fever. Those inhabitants of the village of Sezze living near the marsh suffer from malaria, while those whose dwellings are situated quite near in the vicinity of the hills are not affected. Ships that anchor at some distance from a malarial coast are not apt to be attacked by the disease. According to Vincent and Burot, during the campaign in Madagascar the troops on shore were decimated by malaria, while the crews who for months were on board ship, hardly 300 m. from the shore, were not ill at all. Kohlbrugge reports of the notorious port Tandjong Priok (Batavia), that if ships anchor in the inner harbour for only one night, that time suffices to infect those on board with malaria ; if, however, the ship remains in the outer harbour, the crew, &c., remain healthy.

Moreover, it is known that malaria only rises a short distance above the soil. Even a slight elevation of a few yards above the level of a much-infected marshy soil would suffice to protect one from the infection. Thus the inhabitants of the Pontine marshes during the fever season sleep on platforms erected on piles six or seven yards in height (Bignami).

The air theory is likewise contradicted by the fact that infection ensues most frequently when the soil is damp, not when it is dry and dusty.

Finally, Bignami proves the fallacy of this theory by mentioning that he was never able, in the peri-bronchial glands of persons from malarious districts, to find forms of a parasitic nature, which according to his opinion must have been the case were it possible to inhale the germs of malaria with the dust.

(2) According to the *drinking-water theory*, the infection is brought about by drinking water originating from malarial soil. This theory is supported, on the one hand, by the observation that of the persons living under similar circumstances only those suffer from malaria who make use of a certain water, whereas the others remain free ; and on the other hand that, after improvement of the water supply, the fever raging in certain places disappeared.

These observations, however, are balanced by others which can be used to weaken or nullify this theory ; a few of these are herewith communicated.

The following observation of Boudin [1] is frequently quoted. In July, 1834, three French men-of-war started from Bona (Algiers) for Marseilles. During the voyage a malignant epidemic of malaria broke out on board one, the "Argo," with the result that of a crew of 120 men 13 died, and on arrival at Marseilles 98 had to be admitted to hospital. Investigations resulted in showing that in Bona several barrels of marsh water had been shipped, and its abominable smell and taste had led to much grumbling on the part of the men. The crews of the other ships had been provided with clean drinking water, and not one case of illness had occurred on board these. The power of demonstration of this case is however weakened by the fact that the "Argo," as Boudin adds, had come from a malarious harbour, where it had sojourned some time.

[1] Traité de géographie et de statistique médicale, i., Paris. 1357, p. 142.

The village of Bahrwa, three miles from the Terai (see p. 99) was, according to Roux, severely visited by malaria. The inhabitants derived their water from holes simply dug out of the earth. After these unhealthy wells had been closed and bricked wells, 15 m. deep, had been substituted, the fever disappeared.

Davidson mentions the following communication of Faught's. The troops stationed in Tilbury Fort generally suffer severely from intermittent fever. They take the water they require from tanks that are fed from a neighbouring swamp. The persons at the railway station and the coast-guards, who drink water from a spring, are healthy. While these tanks were undergoing repair the soldiers also used spring water, and during that time there was no malaria amongst them.

Celli relates the following facts amongst others. In Rome malaria now frequently occurs in the suburbs where many new buildings are erected and much soil is turned over, although the water supply is excellent, being conducted in iron pipes from a hilly region 54 km. distant; whereas in the centre of the town, which has a water supply from a malarious district conducted partly through bricked, partly through the porous, tufa, and traversing the campagna, malaria does not occur.

The little town of Sermoneta, which is situated on the declivity of Monti Lepini, facing the Pontine swamps, which formerly had 8,000 inhabitants, has now only 800. This serious decrease may be ascribed to the mortality from fever. In order to counteract this untoward condition the town, in 1884, was provided with a good water supply, nevertheless the cases of death increased during the following years.

The drinking water theory is further contradicted by the results of experiments conducted in this direction. Celli for a period of from eight to sixteen days gave large quantities ($\frac{1}{2}$ to 3 litres) of water, which originated from exquisite malaria soil, to six healthy persons, but with negative results. Zeri's experiments were equally fruitless, and consisted, on Celli's suggestion, in getting nine persons to drink daily, for from five to twenty days, $1\frac{1}{2}$ to 3 litres of water from malarial regions ; moreover, sixteen persons were requested to inhale desiccated marsh water, and finally the water was administered by the bowel to two adults and three children (Bignami). In contradistinction to these negative results there were positive results in one of Ross's experiments, but it carries no weight, for it was undertaken in a fever region, and later repetitions of the same experiment gave negative results. The experiment alluded to was carried out on an Indian native who had never had fever ; it consisted in giving him 1 to 2 drachms of water containing a number of mosquitoes full of malarial blood, with the consequence that eleven days later he developed malaria.

(3) The *mosquito theory*[1] has a firmer foundation than the two first-mentioned theories, but it is by no means new. In olden times (Columella, Varro, Vitruvius) it was believed that malaria was transmitted by the stings of insects, and this opinion was later also expressed by Lancisi. Lately Laveran, Manson, and Ross have especially taken up the mosquito theory again, and at present a great number of the most able investigators—Koch amongst them—are engaged in solving this problem, so that we are in hopes that the etiology of malaria will soon be completely elucidated. According to the present condition of these investigations it appears that the malarial parasites are withdrawn from the human body by blood-sucking mosquitoes,[2] in which they go through further stages of development, and are then again transmitted to human beings by mosquito bites.

However, all species of mosquitoes do not act as intermediary hosts,

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[1] Nuttall in the *Cbl. f. Bakt.*, xxv. and xxvi., gives a representation of the historical development of the mosquito theory.

[2] *Mosquito* (gnat) is the collective name for several related insects which belong to the genuses Culex, Anopheles, Ædes, Ceratopogon, Simalia and Phlebotomus ; they by no means exist in warm countries only, for they occur even in Arctic regions.

but only certain of the genus Anopheles,[1] which is also widely disseminated in Europe. According to the investigations of Grassi, Bignami and Bastianelli, the *Anopheles claviger*, *Anopheles bifurcatus*, *Anopheles superpictus* and *Anopheles pseudo-pictus* are principally concerned in this connection, and this genus appears to serve as intermediary host to various kinds of malaria parasites. The *Anopheles claviger* is the most commonly met with, and is easily recognisable by four black spots on the wings.

Moreover, only the female mosquitoes bite, and their span of life may last weeks and even months. For a few days after every meal they deposit their ova on the surface of stagnant water or in damp places, as a rule where they themselves were born, and from the ova develop larvæ, nymphæ, and finally the winged insects.
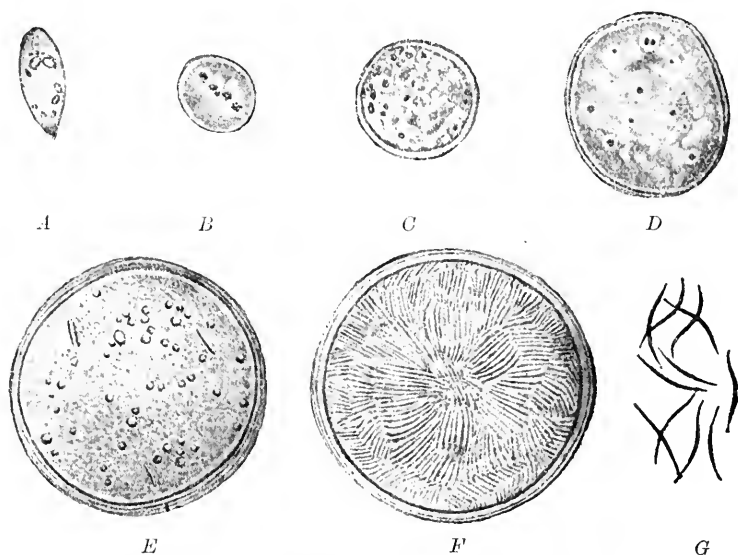
Fig. 19.—Development of the sporozoite cysts in the body of the mosquito. After A. Celli, F, fully developed sporozoite cysts; G, free sporozoites.

The demonstration of the entire cycle of development of the malaria parasites in the body of the mosquito has hitherto not been possible.

The history of the development of two nearly related blood parasites affecting birds—*Proteosoma brassii* (Labbé) and *Halteridium Danilewsky* (Labbé)—of which, likewise, certain mosquitoes are the intermediary hosts, is better known, and by analogy of the same the following picture of the cycle of development of malaria parasites may be made :—

The above-mentioned quickly moving flagellæ (see p. 102) which release themselves from the flagellated bodies are spermatozoa. These originate from spherical parasites which possess a large compact chromatin body and a slightly tinted protoplasm (microgametes, spermoids). Besides this spherical form there is another which is distinguished by having a

[1] The differences between the Anopheles and Culex are described in the *Brit. Med. Journal*, 1899, September 30, p. 869, and deals principally with the auxiliary apparatus of the mouth-organs.

more deeply tinted plasma and less chromatin (macrogametes, ovoids). The spermatozoa penetrate the latter. This process, which was first observed by MacCullum in the halteridium, but on the other hand has not yet been observed in the malaria parasite, takes place in the stomach of the mosquito. After a few minutes the fecundated sphere exhibits a protuberance which gradually lengthens and finally frees itself from the remainder as a small bent little worm. These little worms, which contain chromatin, plasma, unstainable round spots, and pigment also, are transformed after a time into coccidia-like spheres containing pigment (hæmosporidia, sporozoite cysts) which appear on the outer wall of the mosquito's stomach (see fig. 19). These spheres grow during the following days, and secondary spheres form in the same, the secondary spheres in their turn being transformed into a bundle of thread-like formations (sporozoites) each containing a granule of chromatin. The large round forms burst and the sporozoites become free and scatter in the body of the mosquito, but finally they are only found in the two poison glands, which are near to, and are connected with, the sting. This process, first observed by Ross in the proteosoma, was later on observed by the Italian investigators above-mentioned in the malaria parasites also.

The period that intervenes between the time of the infection of the mosquitoes till they themselves are able to convey infection, depends on the temperature, and differs in different malaria parasites; it may fluctuate between one and several weeks.

Ross succeeded in infecting healthy birds through mosquitoes that had sucked proteosoma blood, and the Italian investigators had the same good fortune with malaria parasites. They caused a number of *Anopheles claviger* to suck the blood of a patient with æstivo-autumnal tertian fever. After ten days, having previously examined several of the mosquitoes to convince themselves that the salivary glands contained sporozoites, a healthy man was bitten by three mosquitoes. After twelve or thirteen days this man had a severe attack of typical æstivo-autumnal fever. The mosquitoes were examined immediately after they had bitten, and in two of them innumerable sporozoites were found in the poison glands. From this it seems without doubt that malaria parasites can pass direct from man to the mosquito, and from the mosquito again to man. The parasites, therefore, are beings that have two hosts and alternating generations, a sexual and an asexual one. As the sexual form of development gone through in the mosquito is to be regarded as a higher form than the asexual one in man, the former in contradistinction to the above-used designations must be looked upon as the definitive host and the latter as the intermediary host.

The investigations have hitherto not proved certain points which possess some probability, namely, that parasites might be transmitted from mosquito to mosquito through several generations by the sporozoites being deposited in the ova and thus bequeathed to a new generation. This mode of transmission has been observed in the Texas fever of cattle (see p. 110), which is related to malaria. The signification of the cylindrical dark brown bodies with black outlines, closed at the extremities, which are partly straight and partly curved, and which remained unchanged in water for months, is quite unknown. Ross found these in certain hæmosporidia of the proteosoma in the place of sporozoites, so perhaps they may be degenerative forms of sporozoites. It is, however, not beyond the bounds of possibility that they represent long-lived forms which perhaps might infect the larvæ of mosquitoes, once they reached

the water. As yet it is not known how the sporozoites injected into human beings develop the malaria parasites.

By means of the mosquito theory a series of facts are explained which are not elucidated by the other theories. In regard to malarial infection, the evening and night hours are the most dangerous, being the time when the mosquitoes, which during the day usually stay in the grass and bushes, leave their shelter and come out to torment human beings. An observation repeatedly made is that persons living, that is to say sleeping, on ships, though engaged in business on shore, are much less apt to suffer from malaria than those sleeping on land. As already mentioned above, malaria not rarely possesses narrowly confined centres, and can only rise slightly above the ground ; this may be attributed to the fact that mosquitoes do not move far from the place where they are born, and mostly stay in the deeper strata of the air near the ground. Many protective measures employed in malarial regions to avoid fever serve simultaneously as protections against mosquitoes likewise : as such may be mentioned the kindling of fires when camping in the open air overnight, sleeping with closed windows and in the upper storeys of houses, and the use of mosquito nets. Bignami relates that Emin Pasha, during his African travels, always took a mosquito net with him, and attributes his freedom from malaria to the regular use of the same at night. He imagined that the virus of disease was represented by a corpuscular substance, which is not able to penetrate the net. The immunity, also, of the sulphur miners in Sicily in particular is explained by the mosquito theory, the smell of sulphur having a repellent effect on insects. The theory may likewise explain why European children with tender skins are particularly susceptible to malaria, while the thick-skinned negroes, on the other hand, enjoy relative immunity (see p. 110).

The mosquito theory finds a powerful support in the analogy of blood-diseases occurring in animals, especially as regards *Texas fever* and *Tsetse disease*.

Under the name of *Texas fever* or *cattle malaria* is comprehended a *cattle* disease which is originated by micro-parasites burrowing into the red blood corpuscles ; it occurs in America, especially the south of the United States, in South Africa, German East Africa, Australia, Italy, Sardinia, the lands of the Danube and the south west of Russia and Finland.

The micro-parasite discovered by Smith and Kilborne represents a pear-shaped form in the completely developed stage, which stains moderately well with the usual basic aniline dyes. Generally two such bodies are found lying close together within one red blood corpuscle, and for this reason the parasite is called *Pyrosoma bigeminum*. Besides these completely developed parasites, adolescent forms are observed. Koch found the latter as rod-shaped bodies, frequently somewhat bent, so that they were the shape of half rings or even rings, having some resemblance to the parasites of tropical malaria. Often the rodlets are somewhat thicker in the middle, and between this form and the pear shape all the transitions take place. In cases of Texas fever of acute course these adolescent forms alone are found in great numbers, from one to four being in one blood corpuscle. The slower the course of the illness the fewer of these are found, their places being evidently taken by adult forms only. After recovery from the disease Koch could only find a few parasites of the adolescent form.

The recovery from Texas fever conveys immunity from a new infection even in cases where the disease has been mild. In places, therefore, where the disease is endemic, the cattle have become more or less immune, and suffer but little from it. But if these animals come into touch with cattle from fever-free regions, and are therefore not immunised, the pestilence breaks out amongst the latter after a few weeks. The transmission, however, does not occur direct from animal to animal, but takes place by means of a *kind of tick* (*Ixodes bovis*, Riley), *Boophilus bovis* (Curtice), and the infection, as discovered by Smith and Kilborne and recently confirmed by

Koch experimentally, is caused not by the ticks that infested the sick animals, but by their brood, the larvæ that have escaped from the eggs. In what manner and in what stage of development the parasites pass from the female tick to the larvæ is still unknown.

During the summer months the danger of contagion and the severity of the pestilence is greatest.

The clinical account of Texas fever consists principally of the appearance of *high fever*. The beasts have a high temperature, do not eat, are very exhausted and prostrate, and soon become very thin. Sometimes constipation, sometimes diarrhœa is present. In most, if not in all, cases a symptom occurs which at once awakens a suspicion of Texas fever. This is the sanguineous, dark red or black colour of the urine, which is caused by the mixture of the urine with dissolved hæmoglobin. It is a question, therefore, of *hæmoglobinuria*. In the worst cases the disease has a fatal termination in two to four days. Sudden deaths even, without premonitory symptoms, may occur from rupture of the spleen.

The anatomical changes found in animals that die from Texas fever are:—The blood is seen to be very liquid and pale. The subcutaneous tissue, the muscles and all the organs exhibit anæmia of a high degree and a distinct icteric tint. Small hæmorrhages are present on the inner layer of the pericardium. The myocardium is yellowish-red, dull, soft and brittle, and exhibits sub-endocardiac blood extravasations. The lymphatic glands are enlarged, greyish-red and very succulent. The spleen is much enlarged, being two or three times its normal size, of a black-brownish or red hue and very soft. The liver is also somewhat enlarged, of a yellowish tint, especially on the incised surface; the gall-bladder, as a rule, is quite filled with thick green bile. Microscopically the hepatic cells of the liver, according to Koch, are found to be much changed in the vicinity of the intra-lobular veins; they are no longer pigmented, nor are their nuclei stainable in places, so that they must be looked upon as having perished. Their contours, however, are still distinctly recognisable from the reticular bile capillaries surrounding them, and which are filled with a shiny yellow solid substance which in places resembles a mass artificially injected. Koch regards this condition of the biliary capillaries as quite pathogenic of Texas fever. Moreover the kidneys are enlarged and of a dark brown colour, the medullary substance reddened and permeated with brownish-red streaks, the mucous membrane of the kidney pelvis somewhat swollen and infiltrated in places by small extravasations of blood. Finally, Koch found the mucous membrane of the fourth stomach, the duodenum and the small intestine in parts spotted red.[1]

Tsetse or *Nagana disease* is the name of an illness in Africa to which animals, more particularly cattle, are liable, and which is caused by a certain blood parasite. Koch affirms that this disease is identical with the *Surra* disease of India. Its geographical distribution, as known at present, is India, Burmah, South, West and East Africa. The disease is most often endemic in the marshy valleys near rivers and lakes. According to the observations made in India, it appears especially during the rainy season.

The cause of the tsetse disease, which was discovered by Bruce, is a *species* of *trypanosoma*. The adult is two or three times as long as the diameter of a red blood corpuscle, is of a fish-like form and exhibits lively movements by means of which it darts to and fro between the blood corpuscles. Koch has never observed it within the blood cells. It is colourless, and may be easily stained with aniline dyes. In its adolescence, according to Plimmer and Bradford, it assumes amœboid and plasmodia-like forms (by the coalescence of two or more amœboid forms). It is transmissible with blood in the most diverse animals. The natural transmission of the disease from one animal to the other is by means of *stinging insects*. In Africa it is the *tsetse fly* that causes the disease. On the coast of German East Africa the disease, according to Koch's investigations, is never transmitted spontaneously, no tsetse flies or other stinging insects suitable for transmission being present there. It has not yet been ascertained by what means the transmission is effected in India, but most probably by means of stinging flies also.

The period of incubation, according to Koch's experiments on this point, averages from nine to twelve days.

The disease commences with a rise of temperature, the parasites being then visible in the blood. The animals exhibit rapidly increasing weakness, become emaciated and anæmic, and œdema sets in. In Indian reports, dimness of the cornea and extravasation of blood in the anterior chamber of the eye are mentioned as occurring occasionally. The animals either rapidly succumb to the disease or go through a longer or shorter period of sickliness, during which the parasites periodically disappear from the blood,

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[1] B. Scheube, article on "Texas Fever," in "Eulenberg's Encyklopäd., Jahrbh, viii., 1899, p. 565.

and periodically reappear, until after many months death ensues.   Spontaneous recoveries, according to Koch, do not occur, or are quite exceptional.

On dissecting the dead animals, the lymphatic glands, more especially those in connection with the inoculated spot, are swollen. The spleen and liver are enlarged, and the liver is often in a state of fatty degeneration.[1]

Against the mosquito theory it is urged that in some malarial districts mosquitoes or other blood-sucking insects are rare, or even non-extant, while generally there are great numbers in malarial regions.   Thus in Sierra Leone, according to Duggan, there are but few mosquitoes and these only during a short period of the year, though malaria rages there severely.   A. Plehn reports that in the worst fever centre of Cameroon on the Joss Plain, mosquitoes of every kind, as also other stinging insects, are remarkably rare, and in other places, such as Kibi, are entirely absent.   Proofs of the correctness of such statements are urgently necessary.   Grassi mentions that in Italy he succeeded in confirming the presence of mosquitoes in numerous regions where their existence was denied by the native inhabitants.   On the contrary in some malarial districts the occurrence of malaria is strictly connected with the occurrence of mosquitoes.   Thus in Constantine (Algiers) mosquitoes and fever occur in the valley of the Rummel, and are absent on the high parts of the town.   The same conditions prevail in the Roman Campagna and inside Rome.   The small island Chole in German East Africa is free from mosquitoes and also from malaria.   The absence of malaria in many regions swarming with mosquitoes has no significance ; for besides mosquitoes (and, indeed, certain species of the same) the existence of the malarial parasites also is necessary for the origination of the disease.

The mosquito theory is discountenanced also by the fact that no positive example is known in which malaria has been carried by a sufferer from the disease to a place where there is no malaria but where mosquitoes exist, notwithstanding the frequent change of location of malaria patients.

If the mosquito theory be correct, the long-standing epidemiological acts in regard to malaria must be coincident with the disease.   Based on experiences extending over more than a hundred years, one is justified in accepting that *malaria is connected with the soil of certain tracts of land*, and one is equally positive that the development of the disease depends on two important factors, (1) a relative moisture of the soil, and (2) periodical high temperatures.

In regard to the first mentioned factor, most malarial regions are notoriously marshy districts, or are at least distinguished by a damp soil.   Those marshes partly fed by sea water are particularly dangerous, especially the so-called delta lands and low-lying sea coasts.   The malarial diseases connected with salt water marshes are of a particularly malignant type.   According to Van der Burg, the general mortality in the Dutch Indian army is in coastal regions one and a half times greater amongst the European soldiers and twice as great amongst the native troops than it is in the interior, malignant malaria being the principal cause.   The following kinds of places are very favourable to the development of malaria : the banks of large rivers subject to frequent floods, the margins of lakes, ponds, smaller rivers, brooks, canals and pits ; in countries artificially irrigated for purposes of cultivation (rice), and in valleys at the foot of mountains, such as the Terai on the southern declivity of the Himalayas.   The explanation of this is that stagnant

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[1] B. Scheube, article " Surra," in " Eulenberg's Encyklopäd.," Jahrbb. viii., 1899, p. 563.

or slowly flowing waters form the breeding places of mosquitoes, which use not only fresh water but also sea water in which to deposit their ova.

Malaria, however, may be endemic in places in which there is not a question of marshy soil, which on the contrary is very dry, as in the Roman Campagna, the dry, sterile plateau of New Castile, on the table lands of Persia, India, &c. The dryness of the soil, however, by no means excludes the existence of smaller collections of water, such as puddles, pools, or muddy spots, in which mosquitoes can develop. The same also holds good for the rainless oases of the African Sahara subject to malaria.

The existence of malaria is especially favoured by the *alternate soaking and drying of the soil*, whereas a thoroughly soaked or quite dry soil does not permit of its presence. In the malarial regions of the banks of the Nile, Indus, Euphrates, Ganges, &c., all of which are subject to periodical overflows, the disease always sets in only after the subsidence of the waters. From this circumstance it will be gathered that the mosquitoes thrive, not in large collections of water where they would fall victims to their foes the fish, but in shallow pools where they are secure from them. Should these small puddles be flooded and washed out so that they are transformed into deeper collections of water, the development of the mosquitoes is disturbed.[1] By draining a damp or marshy soil, malaria as well as mosquitoes are made to disappear, and this has been practically experienced hundreds of times.

According to observations made in India by Rogers, a definite connection exists between the variations of *condition of the surface water* and the fever epidemic which are independent of the temperature and the degree of atmospheric moisture. In places where the surface water is usually high the maximum of the epidemic occurs during the period of the rapid sinking of the surface water, while in those places where the surface water is usually low the maximum of the fever occurs when the surface water is at its highest.

The absence of malaria from large marshy districts of warm countries, where all conditions favourable for the development of the disease exist, proves that the swampy condition of the soil is not the sole cause of malaria. Of such places the marshy banks of the Rio de la Plata, which are subject to periodical overflows, and the swampy districts of New Caledonia, may be quoted as examples.

The geological character of the soil is only of importance to the existence of malaria in so far as it influences the porosity of the soil and its capacity for taking up and retaining moisture. No formation, no mineral excludes the absolute occurrence of malaria (Hirsch), yet by predilection it appears on clay soil, and less on chalk and gravel soil.

The *conformation of the soil* on the other hand exercises an essential influence on the presence of malaria, the regulation of the moisture being in the first place dependent on the conformation. Pits, ditches and similar cavities, without corresponding drainage for the rain water, readily afford opportunity for the formation of swamps. In contradiction to these, steep conical hollows from which the deposit of water can flow quickly are most unfavourable to the existence of malaria.

Elevation above sea level has an important bearing. The extent and intensity of malaria, according to Hirsch, as a rule diminishes in proportion as one rises from the level of the sea to higher elevations. The point of elevation at which malaria occurs varies, however, according to

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[1] The breeding places of Anopheles are mostly small collections of water containing algides. The larvæ mostly live on algides. (*Brit. Med. Journ.*, Sept. 30, 1899, p. 869.)

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the geographical latitude. In Germany the limit is 400 to 500 m., in Italy 600 to 1,000 m., the same holding good for the mountainous regions of Corsica, and for the declivities of the Atlas mountains and in high-lying valleys of Lebanon.

In the highlands of Persia, malaria occurs at an altitude of 1,000 to 1,500 m.; in the Himalayas, on the high plateau of Ceylon, and on the eastern declivities of the Rocky mountains, malaria is still extant at a height of 2,000 m., and in the Peruvian Andes it even occurs at an altitude of 2,500 and more.

At these elevations, valleys with but slightly sloping sides and trough-shaped hollows in the high plains form the seat of the disease. The mosquitoes, also, which require warmth and moisture of the soil for their development, are missing at a certain height. The limits for the occurrence of malaria and mosquitoes occur almost coincidently, according to Koch.

Earthworks, such as the clearing of primeval forests, the turning over of virgin soil, the construction of pits, canals, dams, railways and other highways, the building of harbours and fortifications, all have great influence on the presence of malaria; moreover, *the neglect of cultivation of the soil* and the *decay of land previously built on* are conducive to malaria, whereas, on the contrary, a rational culture of the soil causes the gradual disappearance of malaria. Aschenfeldt says: " Only the greatest wilderness or the most complete culture of the land protects a district from malaria." These facts are in accord with the mosquito theory. Changes of the soil of all kinds afford ample opportunities, when it rains, for the formation of small collections of water which may become the breeding places for mosquitoes. These puddles disappear when the ground is properly cultivated, and are seen again when the ground is neglected.

Davidson has lately published an interesting account of the epidemic in Mauritius, which lasted from 1866 to 1869, in which year Réunion was attacked. During the second year of the epidemic the mortality was greater than it had been in the Great Plague of London in 1665. Davidson, however, in his work offers no explanation as to how the disease originated. Perhaps malaria may have been imported by Indian or English soldiers who had previously suffered from malaria in India or elsewhere coming to Mauritius, for Mauritius and Réunion were formerly considered sanatoria for malarial patients; the interference with the natural water courses of the island rendered the low lying parts swampy and provided an enormous number of breeding places for mosquitoes, by means of which the disease gradually spread over the islands.

The *southern states* of North America form a further example of the influence of deterioration of the soil on the development of malaria; during the Civil War the country was uncultivated for years, and afterwards malignant forms of malaria—hitherto unknown—made their appearance.

After changes of soil in consequence of *earthquakes* the appearance of a considerable increase of malaria has frequently been observed.

The telluric influences mentioned explain the fact that malaria appears more *frequently in the country than in the large towns,* and in the towns themselves the suburbs, in which the soil is being disturbed and new buildings are being put up, are more apt to be attacked than the central parts of the town. Sometimes the malarial centres are narrowly confined and limited to a street, a side street, or even single houses. This fact may be caused by local breeding spots for mosquitoes, and neither the air theory nor the drinking water theory would explain it.

Very different is the circumstance of the occurrence of malaria in *uninhabited* regions where mosquitoes could not have become infected from man. The explanation of this is that in such cases other animals

take the place of human beings, and in this connection the bat is particularly mentioned by Dionisi, who found blood parasites closely resembling malaria parasites in these animals. Manson has endeavoured to give another explanation, namely, that the malaria parasites are usually transmitted from mosquito to mosquito, and man only represents an accidental host for them. According to my individual opinion, the occurrence mentioned is by no means a fact actually confirmed, and fresh observations should be collected as to whether malaria can actually be acquired in such places as possess no human dwellings in their vicinity, as, for instance, the primeval forest.

Temperature is the first to be mentioned of the *atmospheric influences* which are to blame for the appearance of malaria. A certain high temperature is necessary for its development. *Cæteris paribus,* its intensity depends on the temperature of the year, and still more on the average temperature of the summer months. According to Hirsch, the temperature registering 15° to 16° forms the limit at which malarial fevers can occur ; those regions in which this height is not attained by the mean summer temperature remain exempt from the disease. The more serious forms are principally observed in warm countries ; in cooler countries malaria generally occurs in the warmer summer months only. Yet the winter epidemics observed in Russia have proved that malaria, under certain circumstances, can develop at winter temperature. These facts are in complete unison with the mosquito theory. A certain degree of warmth (14° and upwards) is, according to Koch, necessary to the development and maturing of the malaria parasites in the body of the mosquito. It therefore follows that the same kind of mosquito may be harmless at a low temperature, but may become dangerous when the temperature rises. The mosquitoes in zones of moderate heat are driven into houses, huts, stables, &c., during the winter, and the parasites then perish. In the spring, however, the mosquitoes re-infect themselves from patients who are suffering from relapses, which thus, as it were, form the connecting link, the bridge, between the fever time of one year and that of the next. The malarial fevers occurring in winter are nothing more or less than relapses of the disease acquired in summer. These will be the more numerous the more distributed the endemic disease in summer.

A great *change of temperature* does not influence the origination of malaria ; a great fall of temperature is, however, of importance, as relapses may be caused by chills.

Atmospheric depressions and the moisture of the ground attendant on the same, are of great importance. As already mentioned, a thorough soaking of the soil is deleterious to the development of the mosquito ; the degree of moisture favourable to such development depends on the nature of the soil. The drier the soil, the more copious must be the amount of rain in order to affect it, while very heavy rain has a deterrent influence on naturally damp soil. In most tropical countries malaria is most severe, and has a larger area, during wet years. These facts are also elucidated by the mosquito theory.

The same holds good as to the influence of the *seasons* on the genesis of malaria, which is dependent on the co-operative effect of temperature and atmospheric depressions. It is the degree of temperature in colder climates which induces the periodical predisposition to malaria, the necessary moisture being generally extant ; in hot climates, on the other hand, the atmospheric depressions favour the outbreak of the disease, the heat never being absent.

In *cooler climates,* according to Hirsch, two periods of marked fre-

quency of disease are observed, one in spring the other in autumn ; the latter is more striking ; and the more severe the malaria, the more severe will other illnesses also be. In summer there is a considerable abatement of illness, and the minimum is attained in winter. The same condition is shown in high-lying or mountainous regions of the tropics and sub-tropics. The climax of the great epidemic or pandemic outbreaks generally occurred during the latter part of the summer and in the autumn. Future investigations will show what relation relapses, the incidental cause for which is furnished by frequent chills, may bear to the spring infection. Celli and Del Pino found in the Campagna that the fevers of March to the end of June were relapses of former infections. Towards the end of June the first infected anopheles were found and their number increased in July and August.

In *sub-tropical regions* the second period of disease which, starting in the summer attains its climax towards the end of the summer and the commencement of autumn, and sometimes goes on till the winter, is more important than the spring period of the disease, so that the latter is frequently non-existent ; there is then only one period of illness attaining its maximum in summer and autumn, the minimum of disease being in winter and spring.

In the *tropics* the prevalence of the disease is connected more or less with the rainy season. Generally the most numerous and the severest illnesses occur in the times of transition from the dry to the rainy season, and from the rainy to the dry season, or during the months after the rainy season ; they occur much more seldom at the height of the rainy season when, in Deli in Sumatra (Martin), and in New Guinea (Schellong) the minimum number of illnesses is notified. In Cameroon, according to Plehn, the rise of malaria follows the depression of the barometer fairly reliably after about a month ; the largest number of deaths, however, takes place at the height of the rainy season. The differences exhibited in this respect by separate places undoubtedly depend on the nature of the soil, and the cause can only be explained by a minute special study of all the attendant physical conditions.

As the different malarial regions of the tropics vary, according to their geographical position, conformation and condition of soil, as to the commencement of the rainy season, its duration, and its influence on the origination of malaria, the *period of fever* in these regions is also very different. Thus the rainy season in Senegambia and on the coast of Guinea falls in June, September and October ; in Cameroon between July and October ; on the Tanga coast in December and January ; in British India between September and December ; in Brazil from April to June ; in Central America from November to May, while in the West Indies it extends through the entire summer and autumn.

The *winds* only play a subordinate part in the development of malaria, but when they blow over marshes or other sources of malaria they may carry the disease to fever-free spots. Rasch observed in Bangkok the inmates of certain houses were, from this cause, attacked by fever during the south-west monsoon. The transmission of malaria, however, by means of winds can only take place over short distances, and hills, woods, and similar hindrances suffice to protect the houses to the leeward from the illness ; this fact is explained by the mosquito theory, for mosquitoes, which are unable to fly far without resting, and which hide in the grass and bushes when it is windy, cannot be driven far by the breeze and are stopped by obstacles. It has already been mentioned that ships anchoring at a short distance from a malarial coast are not attacked by the disease, yet exceptions occur ; thus Brunnhoff mentions that on board the " Freya " off Arica (Peru), two German miles

from land, malaria occurred though there had been absolutely no leave of absence on shore.

Favouring influences are sometimes ascribed to particular directions of the wind. In Italy and Sicily malarial disease increases in extent and intensity when the *sirocco*, the African west wind, blows. According to Hirsch, this is attributable to the thermometrical and hygrometrical conditions of the atmosphere caused by the influence of the sirocco. On the coast of the Gulf of Guinea, the wind blowing from the desert, here called *harmattan*, causes the cessation of malaria (Fisch). On the tropical sea coasts the sea breezes blowing by day have a purifying effect, while the land winds which blow at night convey malaria from the interior to the colonies on the coast.

Cold winds occasion chills, and through these relapses are often originated.

There are several observations from which it would seem that the virus of malaria may be carried from one spot to the other by soil or other inanimate objects, such as clothes, &c. In these cases infected mosquitoes were probably transported with the articles.

Salisbury, according to Hirsch, even proved experimentally the transportability of the virus of malaria. He filled several boxes with earth taken from the surface of a notorious malaria soil, and took these to a very dry district about five (German) miles from the malarial district, situated about 300 feet above the level of the water and where no case of malaria had ever occurred. The boxes were placed on the window-sill of a room on the second story bedroom occupied by two young men, the windows of which were not closed at night. Six days after the placing of the boxes on the window-sill both inmates complained of indisposition, and on the twelfth day one, and on the fourteenth day the other, had his first attack of intermittent fever of the tertian type, which soon yielded to quinine ; while four members of the same family, sleeping in the lower story of the house, had no indication of the disease. A second experiment had the same results ; a room of a neighbouring house, occupied by a young man and two boys, was similarly arranged ; on the tenth day one boy, and on the thirteenth the other, got intermittent fever; the young man remained healthy.

The epidemic appearance of malaria amongst the crews of *ships* on the high seas may be probably ascribed to the invasion of infected mosquitoes, in those cases which, in view of the abnormally long period of incubation (see below) cannot be traced back to previous infection. Hirsch quotes a series of examples of actual ship malaria. The following observation, published by Simon, is particularly interesting : —

In March, 1887, the gun boat " La Vipère " was stationed in the Bay of Halong, and six men of the crew, out of a total of seventy-seven men, of whom none for a considerable time had been on shore, were attacked by malaria. The soil of the bay coast was not marshy, but rather rocky, and the recent temperature had been relatively cool (12 to 15°). From these facts Simon concluded that the infection originated in the ship itself, not from the shore. In the lower hold, where the patients had had their berths, some slimy sand was found, and this part of the ship being near the engines, was very warm. Simon is of opinion that the germs of malaria were in the sand, which had been shipped as ballast and had mixed with the air of the hold. The illnesses ceased after this lower hold had been evacuated, cleaned and disinfected.

In a similar manner the development of epidemics in countries hitherto exempt from malaria might be explained. One may imagine that the importation of the disease may be effected either by infected mosquitoes, which, like locusts, invade entire districts, or, in case of the presence of those species of mosquitoes that serve as hosts to the malaria parasites, the infection may be spread by them through the medium of malarial patients. The epidemics are often preceded by floods, which afford opportunities favourable to the development of the mosquitoes.

From what has been previously said it will be seen that, as a whole, the epidemiological facts in regard to malaria coincide entirely with the mosquito theory, leaving only one or two points to be cleared up.

The *period of incubation* is supposed to fluctuate between a few hours and several months. There are certain instances in which it has been observed that the disease only set in six or even ten months subsequent to the individual leaving the malarious district (Braune and Fiedler). In analogous cases, however, it would be more correct to speak of *latent infection* than of so long a period of incubation. On the other hand, the statements that occasionally the illness breaks out a few hours after arrival merit little attention, in view of the course of development of the parasites. The fact is that in fever regions every feeling of indisposition is, without confirmation, attributed to malaria. From ten to fourteen days may be taken as the average period of incubation ; this is the time observed on board ships which have only held communication with the coast for a short time.

In experimental malaria, the period of incubation according to Bastianelli and Bignami differs in accordance with the different kinds of parasites, and stands in direct ratio to the quantity of blood inoculated. In quartan fever it averages thirteen days, in tertian fever ten days, and in æstivo-autumnal fever three days.

By means of preventive injections of serum Celli and Santori were able to considerably prolong the period of incubation of experimental malaria in animals naturally immune to malaria (buffaloes, horses, cattle).

Race and nationality play an important part in the ætiology of malaria. Though no race or nationality are entirely exempt, still, according to Hirsch, the nations belonging to the Caucasian race (Europeans, Arabs of the Barbary States, Indians) exhibit the greatest predisposition. The predisposition is less marked in the Malayan and Mongolian races ; and least of all in the Ethiopian races. But even in the last named there is not the slightest question of complete immunity, for the Ethiopian is only relatively and partly immune. The thick skin of the negro, frequently also anointed with grease, and the repugnant smell of their bodies affording a certain protection from mosquito bites, partly due to natural selection of the strongest for existence. This is proved by the frequent occurrence of illness and death in negro children.

Koch attributes this immunity to recovery from malaria without quinine. In German East Africa the negroes of Mount Usambara, if they go to the coast, are seized by malaria of a remarkably severe type. Should they recover, they become immunised like the coast dwellers of the same race, whose immunity may be ascribed to the circumstance that their forefathers were immune, and that they themselves had probably had the illness mildly during their youth. The same immunity gradually increasing from the time of their birth is enjoyed by all natives of malarial regions in their home. This immunity, however, is extinguished if they are transported to another climate, even if it be no more unfavourable than that of their own home. In Cameroon, F. Plehn very rarely observed malaria in the native negroes, and on the other hand very frequently observed it in imported negroes. The natural immunity of the natives may be annulled by the unfavourable hygienic conditions under which they live. Thus, according to Roux, in Bengal the natives suffer more frequently and more severely than the Europeans, and Fayrer made the same observation in Bengal.

The *Europeans* newly arrived from Europe are the most predisposed to malaria. When they have been exposed for some time to malarial

influences without falling ill, they, like the natives, acquire a certain immunity.   Complete acclimatisation, however, never takes place.   After a long period of health a remarkably severe attack may set in, while, on the contrary, persons who immediately after their arrival in a malarious region have suffered from a severe attack, are subsequently free from relapses for a long time (F. Plehn).   The immunity thus acquired, however, becomes insufficient, or is lost, if the epidemic increases in severity, as it is also after a long stay in malaria-free districts. Immunity, moreover, only holds good for the locality in which it was gained ; should the person to whom it relates go to other malarial regions his protection from the illness is lost.

The *half-castes* of European and native parentage, in regard to their liability to the disease, take after the Europeans more than after the natives (Martin).

As to the different forms of malaria, Europeans newly arrived from Europe suffer more from severe acute forms and acclimatised persons from chronic forms of malaria.   In Europeans the quotidian or remittent type of fever prevails ; in the less predisposed races the tertian or quartan type.

There is no great difference in *sex*.   Pregnant women are not immune, as was supposed to be the case formerly ; should they develop fever about the sixth month miscarriages or premature births are the result (Edmonds). Parturition has a predisposing effect.   In India, according to Davidson, more women than men die amongst the native population as well as amongst the military.

As to *age*, the largest contingent, according to Schellong, is furnished by the age of childhood and youth up to the thirty-fifth year.   Old folks exhibit the least predisposition, but once attacked run greater risks.   The first years of life are most predisposed to the disease.

Some babies are *born* with malaria, exhibiting at birth an enlarged spleen, a pale cachectic complexion, and œdema of the feet.   De Freytag and Van der Elst, during 1873 and 1878, observed in Atjeh that all newly-born children were suffering from malarial cachexia, and most of them died during the first months of life.   The presence of malarial parasites in the blood of the fœtus of malarial mothers has been repeatedly confirmed (Bein and Kohlstock, F. Plehn).   Winslow reports that the child of a malarial patient suffered from daily convulsions from the day after birth ; the malarial nature of these attacks was confirmed by the discovery of the parasites in the blood, which disappeared after the administration of quinine.   According to Felkin, malaria may be also transmitted by the father, the mother remaining healthy meanwhile.   This author is of opinion that malaria may even occur *in utero*, as evidenced by lively tremulous movements of the child ; it may also be transmitted by suckling.   The possibility of transmission by means of the semen, or by suckling, nevertheless seems to me highly doubtful.

The *constitution*, moreover, exercises considerable influence.   Healthy persons are more capable of resisting the influences of malaria than those of a weakly, anæmic, and nervous temperament.   In strong persons the severe, acute forms prevail ; in the weak—and especially in women—the chronic forms, tending to cachexia, are the most usual (Martin).

According to Dempwolff, the *temperament* is more decisive as to predisposition than the constitution.   He found that phlegmatic persons, religious natures, and fatalists bore the stay in New Guinea very well ; while sanguine persons, those of an ambitious, active nature and persons of a nervous temperament, suffered severely from each attack of fever, fretted themselves beforehand, and mostly had to be sent home ill.

There is, however, an *individual predisposition* which exists, independently of constitutional or other conditions. Perhaps this may have some connection with the fact that certain persons attract insects, such as mosquitoes, more readily than others.

In regard to *occupation,* agricultural labourers, planters, field-workers, gardeners, harbour and canal workers, surveyors, in fact all persons whose occupation keeps them in the open air, are most exposed to malarial influences, and chiefly fall ill from acute affections, while merchants and officials suffer from the chronic forms. Out-of-door workers, however, acquire immunity much more quickly, whereas persons with indoor occupations always suffer from disorders of acclimatisation and soon become anæmic (Martin).

The predisposition is heightened by all *enfeebling circumstances,* such as colds, becoming wet, bodily and mental exertions, emotion, deprivation of sleep, working in the sun, (sun-fever),[1] insufficient food, or food of bad quality (tinned goods), thirst, sexual excesses, opium smoking, other illnesses and incidents (sea-sickness, menstruation, confinement), injuries to the body, operations ; for this reason it is advisable in fever regions to administer quinine prophylactically to persons who have had malaria previous to operation, or on their being wounded.

As already mentioned, *unfavourable hygienic conditions* play an important part. To dwellings, in particular, Schellong ascribes a great significance ; small, dirty, mouldy dwellings are suitable to the propagation of the infection ; the same may be said in regard to damp mat-huts and newly-erected dwellings, whereas roomy dwellings, provided with all hygienic requirements, minimise the possibility of infection. It may be remarked that mosquitoes exhibit a proclivity for gloomy, damp and dark places. According to the same author the *wholesale illnesses* which are wont to appear where earthworks of a large extent are carried on, may be attributed, amongst other favouring circumstances, above all to a faulty condition of the dwellings and to bad food. Examples of such occurrences are afforded by the construction of Wilhelmshaven, the construction of the railway in South Russia, and the building of the Panama canal.

The predisposition to malarial attacks is increased by nothing more markedly than by *previous illnesses once or twice repeated.* For persons who have suffered formerly from malaria quite slight causes suffice to cause a fresh outbreak of the disease—a slight cold, a simple cold bath, a cold shower bath, a slight attack of indigestion, a change of residence, a voyage. Of course, it is impossible to find out if these cases of illness are relapses caused by malaria parasites retained in the body, or new infections. When the illnesses set in a long time after quitting the centre of malaria, in malaria free districts, on the voyage home, or on arrival in Europe, as is frequently the case, relapses must be the cause. Schellong himself suffered from relapses twelve and twenty-six months after leaving New Guinea, having in the meantime resided in places free from malaria. One can therefore never be assured of definite recovery until a few years without illnesses have elapsed. A few persons, indeed, who have lived for a long time in malarious regions suffer more severely

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[1] Under the term sun-fever is understood attacks of fever of short duration, caused by the effects of the direct rays of the sun on the insufficiently-protected head. The rise of temperature averages 38 to 39°, and is accompanied by violent headaches, mostly one-sided, a slight stiffness of the neck, and contracted pupils. It is questionable if this be a question of malaria or sun-fever.

from fever on their return to Europe than they did while abroad, and frequently die of it.

Water cures frequently cause the reappearance of relapses, as has been observed by Glax in Rohitsch, by Kisch in Marienbad, and by Pollatschek in Carlsbad ; the latent malaria parasites in the blood being recalled to activity by the baths, when they again exercise their deleterious effects. F. Plehn made the same observation after treatment by inunction and the use of arsenic.   It is therefore advisable, when possible, to put off energetic cures until complete reacclimatisation has taken place.

In Africa it is a well-known fact that travellers do not suffer during expeditions into the interior, but only have serious attacks of malaria after their return to the coast.   According to F. Plehn, it is the considerable change of climate that causes the outbreak of the disease. Steudel, on the other hand, seeks to elucidate this fact by explaining that during the expedition there is an increase of the metabolism, more particularly an increase of the secretion of sweat caused by the exertion of marches, &c., during the expedition.   By these means the toxic products of the malaria parasites taken into the body are excreted, whereas after the return to the coast the bodily exertions are over and the secretion of sweat less.   Steudel is inclined to think that the relative immunity of negroes is to be attributed to the lively and quite specific activity of their skin, distinctly evidenced by the strong odour of their skins.

Malaria is supposed also to affect domestic animals. The usual intermittent fever, mostly of the tertian type, is seen in horses, asses, mules, cows, dogs, cats, pigs, &c. ; besides these, the pernicious forms, such as cachexia, with splenic tumours and spontaneous rupture of the spleen, are met with. The fact that Di Mattei has proved that no investigator has succeeded in transmitting human malarial parasites to animals does not coincide with the above assertion.

SYMPTOMATOLOGY.

Malaria gives rise to clinical symptoms of great variety.   So distinct are the aspects of the disease that it is possible to group them under headings with pronounced and specific characteristics.   These are :—

(1) Intermittent fever.
(2) Remittent and continued fevers.
(3) Pernicious fever.
(4) Larvated forms.
(5) Malarial anæmia and cachexia.

The present condition of our knowledge does not permit of an etiological division resting on a parasitological basis ; this would be the most scientific, and must be striven for in the future.

1. Intermittent Fevers.

Intermittent fevers, which in the more temperate climates represent the principal form of malaria, also occur frequently in the tropics.   In both, *tertian* and *quartan fevers*, originated by the tertian and quartan parasites respectively are observed ; and they constitute the principal forms of malaria observed in those nations that have the least predisposition to the disease (see p. 118).   Quotidian fever, generally called the tertian-duplex form, is observed in the more temperate as well as in the warmer climates.   According to Koch's investigation, *malignant tertian*, first

described by Marchiafava and Bignami in Italy, is the most frequent type of tropical malaria κατ᾽ ἐξοχήν. [1]

Marchiafava states that 90 per cent. of the cases of fever seen by him in East Africa were of this type. This form is distinguished by the single attack lasting considerably longer than does the attack in ordinary tertian, extending almost over two days and exhibiting on the morning of the second day a more or less marked abatement (see fig. 20). The rise as well as the fall of temperature takes place quickly and the pyrexia is often higher after the remission than previous to it. Should the remission be strongly marked or should the temperature even fall to normal, which sometimes occurs, the fever chart exhibits the appearance of quotidian, in which each second attack is separated by a longer interval. During the further course of the disease the tertian type, influenced by the quinine taken previously, or the commencing of natural immunisation, is apt to assume the quotidian, or an irregular type. It is very rarely in the tropics that fevers uninfluenced by quinine come under observation, for in malarial regions patients coming under medical care have generally previously taken the drug ; it is therefore comprehensible that hitherto this type has not been correctly understood in the tropics, and by most authors it is considered to be the quotidian fever which is the most frequent type.

Fevers with longer intervals, such as quintan, sextan, &c., are not independent forms, but come to pass from the fact that a few parasites remain undestroyed by the quinine and require some time for multiplication sufficient to cause a fresh attack. Ziemann considers this opinion confirmed by the proof that such fevers with long intervals are seldom or never observed after energetic and sufficiently long treatment with quinine. Fevers with irregular intervals are frequently observed in chronic malarial infection.

Prodromal symptoms, according to the statements of experienced observers, are less frequent in tropical malaria than they are in Europe. When present they consist in such general indispositions as are apt to introduce other acute infectious diseases, such as fatigue and a sensation of leaden weight in the limbs, particularly the knees ; disinclination for work and bodily movement, loss of appetite, nervous excitability, frequently evidenced by bad temper, frequent yawning, burning of the eyes, singing in the ears, sleeplessness, toothache, pains in the head and limbs, a sensation of tingling in the fingers and toes, slight feverishness in the evenings and night sweats. Very frequently the same prodromal symptoms and subjective disorders occur in the same person at every attack (F. Plehn).

The assertion of Trousseau and others that the attacks of fever usually set in between midnight and midday, most often in the morning, is not confirmed in the tropics ; the attacks are sometimes observed in the evening. In malignant tertian the commencement of the fever, according to Koch, almost without exception occurs at midday or during the first hours of the afternoon.

The *stage of rigor* is often insignificant, or even entirely absent. Schellong, in New Guinea, observed that rigors were more frequent in

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[1] Celsus (*De medicina Lib.* iii., *Cap.* iii.) gives a good description of malignant tertian fever. Tertianarum vero duo genera sunt : alternum eodem modo, quo quartana, et incipiens et desinens ; illo tantum interposito discrimine, quod unum diem præstat integrum, tertio redit : alterum longe perniciosius, quod, tertio quidem die revertitur, ex octo autem et quadraginta horis fere sex et triginta per accessionem occupat, interdum etiam vel minus, vel plus ; neque ex toto in remissione desistit, sed tantum levius est. Id genus plerique medici ἡμιτριταῖον appellant.

Malays and in Melanesians than in Europeans. In children, the stage of chill is announced by coldness of the extremities, pale complexion, and cyanosis of the lips and nails. During the attacks of fever the children are very restless, toss from side to side, do not sleep, and cry almost continuously.

Headaches are usual, but their location varies. Pains in the back and lumbago are frequent and are not rarely connected with neuralgia of the sciatic and crural nerves. Kohlbrugge, after attacks of fever, observed *pains in the extremities*, more particularly of the legs, which he attributed to the presence of malaria parasites in the bone marrow ; these pains lasted a few days or persisted for weeks.
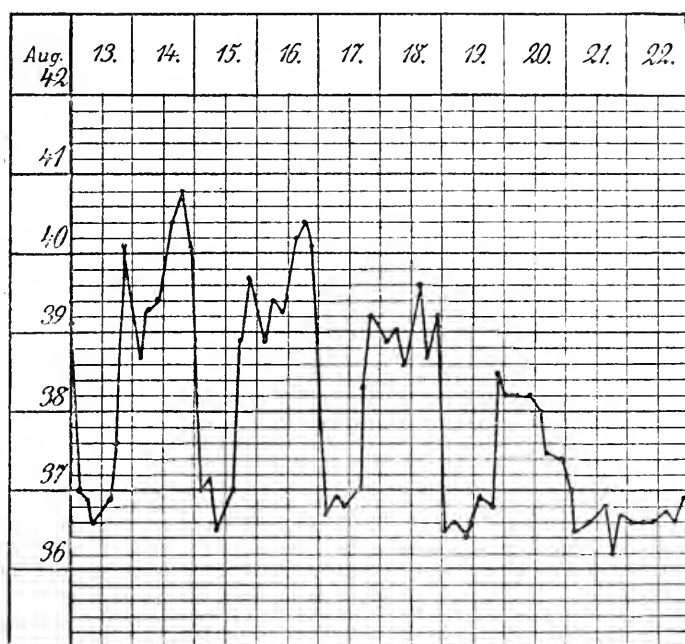
FIG. 20.—Tropical malaria (malignant tertian fever), after R. Koch.

The appetite, as is the case in all forms of malaria, is disturbed occasionally loss of appetite forms the only symptom of malarial infection (Martin).

Often *retching* and *vomiting* and still more frequently *diarrhœa* are present, which tend to quickly reduce the patient's strength. Affections of the stomach and intestines appertain to a certain extent as specific ailments in malaria. According to Ascoli, these are brought about by the elimination of toxic materials through the digestive tract.

In India sanguineous vomit and sanguineous diarrhœa are sometimes observed, and these may even prove fatal (Mason, Clarke). Other hæmorrhages likewise, such as bleeding from the nose, pulmonary hæmorrhages, menorrhagia and petechiæ may occur (Kohlbrugge).

Sometimes the sufferers complain of a *feeling of oppression in the chest ; colds in the head* and *bronchial catarrhs* are sometimes observed.

The *enlargement of the spleen* is frequently quite inconsiderable. In Cameroon, F. Plehn found that the spleen in the majority of cases was not larger than in the cases of typhoid observed in Germany, often even very much smaller. Amongst the remainder distinctly palpable tumours were an exception, even in persons who had suffered much from fever. Schellong observed *dysuria* in nearly all patients. After the attacks, acute *polyuria* frequently sets in with an increase in the secretion of urea, uric acid, phosphoric acid and of chlorides, conveying the idea of the elimination of the malarial virus from the body (Mossé).

The statements of authors in regard to the frequency of the occurrence of *albuminuria* differ considerably, so that in this factor local causes must be taken into account. F. Plehn found albuminuria but very rarely in Cameroon, occurring regularly but slightly only in patients who had previously had blackwater fever, and which Plehn attributed to a slight lesion of the kidney remaining from the former illness. In German East Africa the same investigator observed nephritis more frequently as a complication of malaria. In India, according to Buchanan, albuminuria is but rarely observed, but Wallbridge states that it is frequently seen in British Guiana. In Baltimore, Thayer found albuminuria in 46·4 per cent. of the cases ; in æstivo-autumnal fever in 58·3 per cent. ; in the ordinary forms in 38·6 per cent. ; and acute nephritis in about 2 per cent. In his opinion, malaria probably plays a prominent part in the tropics in the ætiology of chronic nephritis. In Georgetown (Demerara) where malaria rages severely, Daniels states that in no less than 228 *post-mortem* examinations out of a total of 926, the kidneys were found to be diseased.

Often in intermittent as well as in remittent fevers *herpes* and *urticarial eruptions* occur. In rare cases a few observers, such as Franck and Empis (according to Roux) and lately Rasch, have observed that the urticaria affected the larynx, causing dyspnœa with stridulous breathing and oppression (urticaria laryngea malarica). *Erythema nodosum* has been observed (Boïcesco, Moncorvo), attacking more especially women and children. During the attacks of fever the nodules become painful, swell and become reddened, and again become paler towards the end of the attack.

The intermittent fevers, according to Davidson, often assume a sthenic character in healthy Europeans who have only been in the tropics a short time, evidenced by violent rigors, severe vascular reaction, intense headaches, violent delirium, and severe bilious vomiting. In weak badly nourished natives, on the other hand, an *adynamic* condition obtains, which is more dangerous than the sthenic condition ; the rigor is slight or entirely absent, the fever is low, the skin pale, the pulse slow, weak and irregular ; giddiness, stupor and great prostration are present, and the patients are also much exhausted during the intervals.

2. Remittent and Continued Fevers.

Europeans in particular are often liable to remittent and continued fevers in the tropics. These probably always develop from malignant tertian fever, and it is possible that neglect and the influence of unsuitable treatment by quinine have something to do with it ; at times it is observed that intermittent fever precedes and follows remittent fever. The transmission is effected by the prolongation and conjunction of single attacks, or by these being superimposed and therefore mixed one with the other ; or finally that they multiply in consequence of the presence of several generations of malaria parasites of various ages.

Certain intermediate forms occasionally occur, and the temperatures exhibited are occasionally so irregular that one is embarrassed how to refer them to any definite type of fever. Rigors and splenic enlargements are frequently absent.

Other symptoms of the disease are also very changeable. The subjective appearances are often remarkably few. For the most part they consist of gastric disorders, headaches and a feeling of general indisposition, loss of appetite, pain in the epigastrium, heartburn, nausea, eructation, vomiting. Diarrhœa is rarely absent and may become dangerous, especially in children. Slight jaundice often sets in (febris remittens biliosa). Moreover, slight bronchitis is a frequent accompanying symptom. In longer lasting cases, bleeding from the nose and other hæmorrhages, especially in the skin, may be met with. In serious cases the fever assumes a typhoid or adynamic character, stupor, delirium, restlessness, obstinate insomnia ; or, on the other hand, torpor sets in, the tongue becomes dry and foul, the torpor passes on into coma, or the temperature falls to subnormal, the patient becomes apathetic and the most severe prostration ensues, constituting so-called pernicious fever (see p. 128).

The period of the duration of remittent fever fluctuates between three days and three weeks, sometimes it even lasts longer. Towards the termination of the illness the remissions are longer and finally become actual intermissions. A sudden fall of temperature, however, may also take place.

Martin, during convalescence, observed several times a remarkable defect in the memory, which was mostly only arrested by a voyage to Europe. Amongst the Chinese the same author frequently saw serious forms of insanity, accompanied by suicidal tendencies.

Quinine usually has but little effect on remittent fevers, and good results are not attained immediately, even on change of climate. The observation made by Martin and Fuhrmann is interesting, namely that recovery from an attack of remittent fever leaves a certain immunity from further malaria, in contradistinction to intermittent fevers. Typhomalaria is also to be counted in this group of malarial fevers.

Typho-malaria.

Synonyms : *Malaria typhosa, Malaria-typhoid, Typho-malarial fever, Fivère typho-malarienne, Fièvre typho-palustre, Fièvre typho-paludéenne.*

Typho-malaria, which was first described by North American physicians, occurs not only in the tropics, but reports of the disease have come from North America, China, Japan, Algiers, Wallachia, South Russia (where it was seen by P. Werner during the construction of the railway of Samara-Orenburg) and even from Königsberg (Schellong). Overcrowding, insanitary conditions, insufficient food, and bad drinking water, all play a distinct part in its ætiology. It is therefore observed to appear by predilection in campaigns.

Typho-malaria is distinguished by the fact, that in addition to remittent or intermittent fevers suddenly setting in with rigors, *typhoid symptoms* appear ; these consist of diarrhœa, pain in the cæcal region, flatulence, a dry brown tongue, roseola, more or less marked unconsciousness and delirium ; pain may be observed in the hepatic region, with enlargement of the liver and even slight icterus. The vomiting of bilious material is, moreover, a fairly constant symptom. Schellong also mentions hiccough as a frequent and troublesome symptom. The period of the illness varies between one and three weeks or more. Death may ensue from coma, or in consequence of perforation of the intestine, followed by peritonitis.

According to my personal observations made in Japan, I can distinguish two forms of typho-malaria. The cases appertaining to the first form resemble simple typhoid during the first weeks. During the third or fourth week the fever generally becomes intermittent, and severer attacks of fever, mostly coming on in the afternoon or evening, and terminating in the night or morning, set in; these attacks are often introduced by rigors, followed by heat and perspiration, and may be repeated in a regular or irregular type.

In the second form, the fever from the commencement exhibits a very marked remittent or intermittent character. The fall of temperature is occasionally accompanied by the appearance of perspiration, while the rise takes place with rigor, accompanied by pyrexia.

The *spleen* is enlarged to a greater extent than is the case in simple typhoid. Usually, also, a distinct or even considerable enlargement of the liver is observed. These swellings often persist long after recovery, and only disappear gradually in the course of weeks and months, as I was enabled to confirm on my own person, having suffered from a similar attack of typho-malaria in Japan in November, 1879.

As to the remaining symptoms, the intestinal disorders are usually subordinate, as is also, according to my observations, the case in Japanese typhoid and in tropical typhoid generally. The intestinal symptoms are either copious diarrhœa or constipation; the cerebral symptoms, as a rule, are but slight, or entirely absent. I have never missed seeing roseolar spots; they usually set in about the middle of the second week.

In the cases observed by me the disease always had a favourable termination, the fever generally ceasing in the third or fourth week. Most of the American observers of typho-malaria also state that death seldom resulted therefrom, while, on the other hand, a high mortality is reported by other observers. In thirty cases recently compiled by Lyon, the mortality was given as 33·3 per cent.

I found that quinine had no influence on the duration of the fever.

There is no doubt that various kinds of illnesses are confounded with typho-malaria. In actual typho-malaria—and to this type belong the cases observed by me in Japan—there is a *combination* of *malaria* and *typhoid*, the sufferers being either simultaneously attacked by both illnesses, or in such as have previously had malaria the malaria parasites latent in the body are roused up by the appearance of typhoid and the character of the disease is modified. Malaria is indicated especially by the course of the fever and the great enlargement of the liver and spleen; typhoid is indicated by the roseolar rash, and also by the resistance to quinine. Sometimes the malarial and sometimes the typhoid character predominates, so that the French distinguish *malaria-typhoïde* and *fièvre typho-malarienne*. The accounts of the disease, therefore, vary considerably. The simultaneous existence of two infections, the possibility of which has been scouted, by no means stands alone; the simultaneous occurrence of measles and scarlet fever, scarlet fever and small-pox, typhoid and recurrent fever, &c., has been repeatedly observed.

Lately, the proof of the simultaneous existence of the two infections has been furnished by Vincent, Namack, Lyon, Craig and others, by the demonstration of malarial parasites in the blood and typhoid bacilli in the intestinal canal and in the spleen, and also by the positive result of the Gruber-Widal serum reaction in typho-malarial patients.

The term typho-malaria is, however, frequently applied erroneously to pure malarial fevers which have a course more or less resembling typhoid, and also to simple cases of typhoid. A. Plehn, in Cameroon,

and Dock and Miller in Texas, proved that the illnesses usually so des-
ignated in those places were nothing but typhoid. Probably also Malta
fever and other illnesses, the nature of which is not recognised, are called
by this term. In China (Amoy, Foochow, Shanghai, Cheefoo, and
especially on the Kung-tung-tao Isles) there occur, according to Gärtner,
some very malignant fevers which are neither typhoid nor malaria, but
affections *sui generis*, and which in these places are designated as typho-
malaria. It is therefore necessary that the disease named typho-malaria
will in future be pronounced only when, by the aid of micro-biological
examination, malaria parasites are found in the blood, typhoid bacilli in
the stools, and when the Gruber-Widal's serum re-action [1] is elicited.

Besides the above-mentioned fevers, a series of other remittent and continued fevers
are described in warm countries and especially in India, which in their symptoms and
course are very similar to malaria and typhoid. The following are distinguished:—

(1) Non-malarial *remittent fever* to which, according to Crombie, natives are espe-
cially liable,[2] is most frequent in persons under 30 years of age, and is often observed
in children. It sometimes commences insidiously like typhoid. The fever, during
the first few days, is markedly intermittent, but no malaria parasites are found in the
blood, and quinine has no effect. After the first three days the fever becomes con-
tinued, from 40-40·5° with remissions of 0·8-1·4°. Severe cerebral symptoms are also
present; with delirium, coma, enlargement of the liver, bilious diarrhœa, and may
be also slight icterus. The spleen is not enlarged. About the eighteenth to the
twenty-fourth day, hypostasis supervenes in serious cases, and death not infrequently
ensues. In cases with a favourable termination, the fever continues longer, lasting on
an average six weeks. Relapses occur after a week of apyrexia, but are not usual.
Crombie is not of opinion that this fever is identical with Mediterranean fever. The
Gruber-Widal serum reaction does not, however, appear to have been tried.

Van Tunzelmann[3] found crescent kidney-shaped and peculiarly formed bodies in
the blood (shiny, with double contours situated in the red blood corpuscles) in non-
malarial fever; these he designated *medusa sanguinis hominis*; the discovery, however,
lacks confirmation.

(2) So-called *continued fever*. This type, according to Davidson, commences sud-
denly; the temperature attains a considerable height, symptoms of the nervous and
vascular systems predominate and apyrexia sometimes ensues quickly; but this is not
always the case. This illness, which is more frequent in Europeans, especially those
newly arrived, than amongst natives, averages a duration of about a week.

Crombie, besides the *simple continued fever* of one or several days' duration,
distinguishes "city continued fever" and "double continued fever."

City continued fever occurs more particularly in the large tropical and subtropical
towns, especially in natives, and is known locally as "Calcutta" fever, "Bombay"
fever, &c. It is a mild fever lasting from two to four weeks, with an average dura-
tion of three weeks (three week fever), it is of a typhoid type, but without specific
typhoid symptoms. Crombie regards it as mild typhoid; at *post-mortem* examinations
he several times discovered oblique intestinal ulcers (differing from typhoid ulcers,
which run parallel with the greatest diameter of the axis of the intestinal canal). The
serum reaction test does not seem to have been applied.

Double continued fever was observed by Manson in South China. There is an initial
fever stage of ten to fourteen days' duration, followed by a three to seven days' relative
or absolute apyrexia; then another fever period of about ten days, and this is followed
by convalescence. In the first as well as in the second fever the temperature may rise
to 40° or 40·5°. Besides headaches there are no particular symptoms nor complications.

Chassiotis[4] (Athens) whose description of continued fever, however, corresponds
more to that of remittent, found diplococci of varying size, some oval, some round, and
some crescent-shaped in the blood, these exhibited slow movements. He was never

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[1] The significance of the Gruber-Widal reaction is somewhat limited inasmuch as
it is exhibited only in the second week of disease, while on the other hand it is still to
be seen months and even years after the disease, and in some rare cases is not to be
observed at all. The negative result of the proof by agglutination does not therefore
exclude typhoid while the positive result affirms it.

[2] *Brit. Med. Journ.*, 1898, September 24, p. 862.

[3] Medical Report of the Imperial Maritime Custom of China for the half year
ending September 30, 1896.

[4] *Fortschritte der Medizin*, xii., 1894, No. 22, p. 853.

able to confirm a change in Peyer's patches or the mesenteric glands, such as takes place in typhoid. The spleen was seldom swollen, but the liver was always enlarged. In a few organs pigment was met with.

(3) "*Ardent fever*," according to Davidson, is a form of fever which occurs particularly in dry and sterile districts during the warmest summer months, and mostly occurs in persons who have been working or marching in the sun. The symptoms are: burning heat of the skin, thirst, an accelerated strong pulse, severe headache, flushed face, restlessness, a dry tongue, nausea, vomiting, constipation and pains in the back. Sometimes the brain symptoms, and sometimes the stomachic and hepatic symptoms predominate. There is giddiness, sleeplessness and delirium, which may terminate in coma, or bilious vomiting, bilious diarrhœa and icterus, and death may ensue from exhaustion. The period of the illness varies from a few days to a month; in medium cases it averages six to nine days.

The "*fièvre dite bilieuse inflammatoire*" of the French is identical with "ardent fever." According to Nogué,[1] the disease has two very marked periods of fever. The first lasts between four and six days. The temperature rapidly rises to over 40°, sometimes to 41°, and fluctuates between 39·5° and 41°. Between the fourth and sixth day the temperature quickly falls to 38·8°, 36·8° and even to 34°. It then remains stationary for about twelve hours and then again rises to 38·8° to 39°. At this height it remains between eighteen and thirty-six hours or longer and then becomes normal.

According to Crombie simple continued fever (thermic fever) ardent fever (siriasis) and heat apoplexy are different degrees of the same condition and are caused by labouring or marching in the heat. Simple continued fever may, however, ensue in consequence of taking cold.

(4) "*Low fever*" is, according to Crombie, a form of fever which is characterised by low temperatures, these mostly averaging 37·7° to 38·6°, and Europeans only appear to be subject to it. It begins insidiously with slight indisposition and loss of appetite; there are no specific symptoms. It may last for many weeks or months and is influenced neither by quinine, arsenic, nor other drugs, but generally yields at once to change of climate (sea, hills). It is supposed to be caused by a disturbance of the heat centres. Cousland, who also observed this illness in China, regards it as malarial.

(5) Homen, Brazil,[2] describes as "*bilious remittent tropical fever*" an illness which has no connection with intermittent and yellow fever; it appears especially during the summer, and almost exclusively affects healthy persons, who have committed excesses in food or worked in the heat of the sun. It is distinguished by high fever setting in with a severe rigor, vomiting, diarrhœa, jaundice (setting in on the second day) considerable enlargement of the liver and spleen, albuminuria, stupor and occasionally hæmorrhages (setting in towards the end of the first week), hæmaturia in particular.

The cases ushered in with hæmorrhages mostly have a fatal termination on the eighth or tenth day, while in those with a favourable termination convalescence sets in after fifteen to twenty days.

(6) *Boo-Hoo-fever* is the designation for an illness occurring in Honolulu amongst the American troops. According to Robinson [3] this fever sets in soon after the arrival of the men, and like influenza, is indicated by pains in all the limbs, especially in the back, severe headaches, coated tongue, loss of appetite, constipation and mild fever, mostly without rigor. General depression and low spirits are almost constant and seem characteristic of the complaint. The soldiers lose all courage and interest in their duties and have only one desire, namely, to be sent home. This condition, however, is only of short duration and after two or three days the patients have regained their usual health.

This illness is regarded as climatic, and is attributed to the new climatic influences to which the organism has been exposed. Probably, also, home sickness has something to do with it.

Perhaps the microbiological investigations of the future will elucidate the nature of these illnesses.

3. Pernicious Fever.

(Febres intermittentes perniciosæ s. comitatæ.)

Under certain exceptional circumstances when malarial disease affects children, aged people, or persons who have been enfeebled in other ways,

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[1] *Arch. de Méd. Nav.* 1897, December, p. 454.

[2] *Medical Age*, 1895, Nos. 11 and 12 refer to *Cbl. f. inn. Med.*, 1895, No. 52, p. 1,267.

[3] *Journal of Tropical Medicine*, December, 1898, p. 141.

benign forms may take an unfavourable course. In discussing pernicious fevers, however, such cases are not taken into account. The term pernicious fever is employed to indicate those cases which immediately assume excessively serious symptoms which endanger life, and may lead to death in a few days, or even hours. The symptoms are induced, partly directly through malarial intoxication, partly through mechanical disturbances in the circulation of the blood, and are manifested either by a remarkable intensity of the usual malarial symptoms, or by disturbance of important organs. In the latter case perhaps mixed infections have something to do with the condition, the nidus for other micro-organisms being prepared by malaria parasites and their toxins.

The pernicious symptoms sometimes set in quite suddenly during the course of a seemingly mild attack of intermittent fever, a pernicious attack immediately following an ordinary attack, which, however, only causes death after several relapses; sometimes the change from benign forms into malignant takes place by means of gradual aggravation of the symptoms of disease.

The pernicious forms are mostly originated by the *parasites of malignant tertian fever*.

The type of fever may vary considerably; being sometimes intermittent, sometimes—and this is particularly the case in the pernicious forms of the tropics—remittent, continued, or irregular. In rare cases the pernicious forms may also begin without fever, and may run a feverless course during the entire period of the attack, the temperature being even sub-normal. According to Pampoukis, these afebrile attacks are far more dangerous than the febrile attacks.

Certain external and individual idiosyncrasies occasionally have an influence on the *form* of pernicious fever. In hot months the nervous system and the digestive canal are by predilection the seat of the lesions, and in cold months the respiratory organs are affected. The disturbances frequently have their seat in organs that are or have been affected pathologically in some way, or that may have been injured; as an instance, cerebral symptoms set in subsequent to injuries of the skull through a fall or fit, after sunstroke, emotion, or the partaking of alcohol to excess (Hertz).

Certain forms often prevail in certain localities. According to Laveran the choleraic form is frequent in Cochin-China, but rare in Algeria. In Guiana the algide form is frequently observed, and in Algeria and Madagascar the comatose and delirious forms. On the west coast of Africa hæmoglobinuria is the chief representative of the pernicious forms of malaria.

The mortality in pernicious fevers varies according to place and season, but it is always high.

Pernicious fevers are, as a rule, preceded by attacks of milder forms of malaria; they are not generally observed as primary illnesses. The following forms of pernicious fevers may be distinguished:—

(1) The *algide form* (febris intermittens perniciosa algida).

During an attack of fever the body suddenly becomes as cold as ice. The temperature in the rectum is, however, increased, in the axilla it is about 38°, and the patients complain not of cold but, on the contrary, of burning heat (Mannaberg). The skin is pale, livid, covered with cold perspiration, and has lost its elasticity. The pulse is small, thready, irregular, and frequently slows to forty beats per minute; respiration is superficial and slow; the voice becomes weak and hoarse, but consciousness is maintained. The algidity may set in with intermittent,

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remittent, or even sub-continued fever, though itself not intermittent. Once it has set in it terminates within a few hours, either with recovery or death, the latter being the rule. The algide is one of the most treacherous forms of malarial infection.

Algidity is probably originated by the effect of the virus on the vaso-motor centres, and it occasionally co-exists with the choleraic form.

(2) The *diaphoretic form* (febris intermittens perniciosa diaphoretica).

In this form perspiration is excessive and prolonged; the skin, however, is icy cold and there is a tendency to swoon. The pulse is weak and accelerated, respiration is superficial and irregular, and the urine is frequently suppressed. Death frequently occurs during the first attack.

(3) *Malaria-collapse* (febris intermittens perniciosa syncopalis).—A more or less acute condition of collapse sets in, sometimes during the stage of initial rigor; sometimes it follows upon several typical attacks of inter-mittent, or sometimes even during the course of an attack of remittent or irregular fever. The patient faints away, and the pulse becomes accele-rated and small, or quite imperceptible. The faint may deepen to a *typical trance*, lasting several hours, in which the patient may lie absolutely motionless with his breathing stopped, his pulse extinguished and the beats of his heart scarcely recognisable, though in the meantime he is sometimes quite conscious. Death occurs in this stage, or the patient may rally when perspiration appears, generally however, only to succumb to one of the subsequent attacks.

(4) The *comatose form* (malaria comatosa, febris intermittens comatosa). —This form is usually announced by the setting in of cerebral symptoms, such as severe headaches, giddiness, restlessness, apathy, somnolence, and muscular tremors during an attack of intermittent or remittent fever. These symptoms gradually increase, and the patient sinks into a soporific state, and becomes comatose after delirium and convulsions have been present. The pulse in this condition is very frequent, not coinciding with the height of the temperature; respiration is likewise quickened, becoming at times bronchial, at times sobbing, and occasionally even exhibits Cheyne-Stokes' phenomenon (Schellong); the pupils are fixed and are sometimes dilated, sometimes contracted, while the corneal reflex is generally maintained. The coma may last several hours, or for one or even several days, may exceed the period of fever. Consciousness then returns, often with the appearance of profuse perspiration, though the patient is still confused and feeble, and complains of headache and giddi-ness which either gradually decrease or again increase before a fresh attack. In other cases the coma deepens into death. If recovery ensues, disorders, such as a certain obtuseness, disorders of speech, paresis of single limbs, contractions, &c., may remain for a considerable time, or even during the entire life.

Schellong found that splenic enlargement in this form of illness was but slight, or even entirely absent. According to F. Plehn's experiences in Cameroon this form of malaria appears by predilection as an immediate effect of the influence of the sun, or as an immediate concomitant. By examinations of the blood it is difficult to distinguish it from sunstroke or meningitis caused by sunstroke. It has also been observed that evidence of malarial infection follows undoubted heat-stroke after consciousness has returned.

The apoplectic form is a variety of the comatose form in which the coma sets in suddenly; and occasionally also paralyses, mostly hemiplegic, more rarely monoplegic, are observed; these usually appear while full

consciousness is maintained. According to Landouzy hemiplegia is very frequently connected with aphasia. In some cases the paralyses come and go with several consecutive attacks; being thus actually intermittent.

(5) *The Delirious Form.*—After being preceded by the usual head-aches, giddiness, singing in the ears, restlessness and sleeplessness, delirium, which exhibits every transition from the mildest form to the most violent maniacal attacks, sets in, and in serious cases may last a few hours. Death may ensue from sudden collapse setting in during the attack, or by the delirious form assuming a comatose type. In cases with a favourable termination the patient falls asleep and the sleep leads to recovery. A repetition of the attack usually has a fatal termination.

Mild degrees of delirium are sometimes observed at the climax of the fever after mental exertions, or in drunkards, without any importance being attachable to them.

(6) The *convulsive form* (febris intermittens eclamptica, epileptica, cataleptica, tetanica.)

In children, during the hot stage of fever, convulsions are frequently observed, and these are generally accompanied by somnolence or coma. In tropical malarial regions, malaria is the most frequent cause of eclampsia in children (Thornhill). In lying-in women also, the pure convulsive form likewise occurs (Roux), otherwise, however, it is very rare in adults. In the comatose form, on the other hand, sometimes trismus, squint, cramp of the pharyngeal muscles, tetanic contractions, as also clonic spasms of the extremities are observed. *Febris intermittens hydro-phobica* also belongs to this variety and attends every attempt to swallow water, or the mere look of water causes tonic spasms commencing in the pharyngeal muscles and spreading gradually over the face, neck, and finally the entire body (Watson).

The termination in these forms is mostly unfavourable, death ensuing in the first or in one of the following attacks. In the case of children who escape with their lives, Davidson sometimes observed that chronic epilepsy and mental disorders developed later.

(7) The *cardialgic form*. This is characterised by the occurrence, not only of algide symptoms, but by the setting in, during an attack of fever, of remarkably severe pains in the epigastrium, attended sometimes also by hiccoughing and vomiting. The abdomen in the meantime is mostly retracted and very sensitive to pressure.

(8) The *choleraic form* (malaria cholerica, febris intermittens per-niciosa cholerica). This form which, according to Martin, has a course without any attendant rise of temperature, bears a great similarity to Asiatic cholera and mostly ends rapidly in death. The symptoms exhibited in this form are severe diarrhœa and vomiting accompanied by burning thirst. The vomit has usually a bilious colouring. The watery evacuations of the bowels also, notwithstanding their frequency and copiousness, usually remain coloured and until death retain a somewhat fæcal odour. Frequently, in consequence of being mixed with blood, they appear reddish. Rice-water stools, according to Fournier, are never observed. The patient quickly collapses under these symptoms. The face becomes pale, the pupils dilated, the lips and nails become blue, the skin is covered with cold clammy sweat, the extremities and abdomen feel as cold as ice, the pulse is small and frequent, the breathing accelerated, oppression and præcordial agony are present, the secretion of urine is diminished or suppressed, the voice fails, painful convulsions of the lower extremities set in and death takes place apparently by asphyxia. Consciousness is often maintained until the last moment.

This form occurs in cachectic persons and also in patients who have never previously suffered from malaria. In persons suffering from cachexia it is according to Martin absolutely fatal, while of the others about 25 per cent. under suitable treatment may be saved.

(9) The *dysenteric form* (malaria dysenterica, febris intermittens dysenterica). This form also occurs beyond the tropical zone. It has been observed by Debio in the lower regions of the Danube and by myself in Japan. It is generally introduced by diarrhœa, more or less serious, which may have been brought on by chill, errors in diet, &c. In one of my cases a vermifuge (decoctum granati) was the incidental cause. The stools at first are copious, fæcal, mixed with blood and mucus, and their evacuation is attended by tenesmus. During the course of the disease they become more frequent, with increasing tenesmus, while the fæcal material decreases, and the stools at last consist merely of blood and mucus. The average number of stools in twenty-four hours is twenty or more; in serious cases they become so numerous that they can no longer be counted. In addition there are severe pains along the tract of the colon, these being worse in the region of the umbilicus; the pain is increased before each evacuation and by palpation of the abdomen. I was not able to confirm the statement of other observers that the dysentery increases during the paroxysms of fever, and decreases or even quite disappears during the apyrexia; in my cases the dysentery persisted throughout. The types of fever observed in this form are usually the quotidian or tertian, but in my experience the quartan and quotidian may be present.

If no improvement in the condition is effected by suitable treatment or change of climate, the patients rapidly become emaciated, and present a piteous appearance, which is not inappropriately compared by Werner to the appearance presented by atrophic sucklings. The evacuations, still consisting of blood and mucus, become discoloured, serous and of a cadaverous odour. The patients finally perish from exhaustion, after the illness having sometimes existed for months (Martin).

In children who, according to Martin, are frequently attacked by this form of malaria, the disease is less malignant, being with them more chronic and often appearing recurrently.

It is probable that in the dysenteric form of malaria, there is the question, in at least a part of the cases, of a mixed infection. A satisfactory reply to this problem will, however, not be possible until the ætiological factors of dysentery are settled.

(10) *Pneumonic* malaria (malaria pneumonica, febris intermittens pneumonica). This form, also, is not peculiar to the tropics; I have seen it not only in Japan but even in Germany, where, as assistant in Wunderlich's clinic, in Leipsig, I treated a case in 1877.

The disease, as a rule, begins like an ordinary intermittent fever, with or without rigor. The fever is mostly intermittent and, according to my observations, exhibits the type of quotidian or tertian or duplex tertian fever. After a few days it, not rarely, assumes a remittent type, and the fall of temperature may ensue suddenly or gradually.

As a rule, simultaneously with the fever pulmonary symptoms set in, with shortness of breath, pains in the chest, cough and expectoration. Sometimes already, on the first day of disease, a pneumonic infiltration is perceptible by percussion and auscultation. The lower lobes appear, by predilection, to be attacked. In a case examined by me *post mortem*, the entire right lung and a large portion of the left lung were affected. The expectoration is sometimes mucous, sometimes purulent, with a mix-

ture of blood; sometimes, as occurred in my cases, it has a characteristic pneumonic appearance.   During apyrexia occasionally an abatement, or even a complete subsidence of the symptoms, subjective and objective, takes place; in other cases, on the contrary, they remain stationary and increase in intensity during the paroxysm of fever.   The disease is usually accompanied by diarrhœa.

The termination of pneumonic malaria is, when suitably treated, not rarely a favourable one.   On the other hand, the patients may succumb to collapse after four to six attacks.   In the most serious cases the disease, according to Giampetro, exhibits from the very commencement the stamp of pernicious intermittent fever.   The fever is remittent or subcontinued, the local symptoms soon attain a marked degree, and somnolence, delirium, tremor of the extremities, or the most extreme exhaustion, &c., set in ; in other words, the complex symptoms of so-called typhoid pneumonia obtain and the disease has a fatal termination.

Ascoli calls attention to the fact that in patients who have died of acute pernicious fevers it frequently occurs that the autopsy reveals pneumonia which, during life, was concealed by the other symptoms of disease.   He therefore, like Morehead, recommends the minute examination of the lungs in such cases.

Heinemann, in Mexico, observed croupous as well as broncho-pneumonia as a consequence of malarial infection. Croupous pneumonia he found relatively more rarely, but the broncho-pneumonia frequently led to phthisis if quinine was not administered long enough and at the proper time.

Opinions are divided as to the nature of pneumonic malaria.   According to one view it is a question of a particular localisation of malarial infection.   According to the other view it is a complication, the predisposition to which is furnished by malaria.   According to F. Plehn the body, the powers of resistance of which have been damaged by the long-lasting effect of malarial fever, easily falls victim to a number of other diseases.   On the other hand, the injury caused to the body by external influences, or other kinds of infectious diseases, affords an opportunity for the development of the permanent forms of malaria parasites, lying latent in the body; by the chemical changes of the nutritive media (blood), the latent malaria parasites are enabled to develop and become active.

There seems no doubt that pneumonia may occur in conjunction with malaria.   My opinion, however, is, not that the pneumonia as described in this form is a complication, but that it represents an expression of the malarial infection itself; this opinion is strengthened by the fact that, as in malaria dysenterica, the commencement and termination of the fever and the local symptoms are simultaneous, and that the favourable influence of quinine on the entire process of disease is beyond doubt.   It should be the endeavour of future micro-biologists to throw light on this subject.

Martin, in Deli (N.E. coast of Sumatra), where, according to his experience, there is no tuberculosis, observed seven cases in which *there was local lung trouble of a destructive character.* The patients with remittent or intermittent fevers complained of pains suddenly setting in on the left side and a tormenting irritation causing a cough; but, excepting splenic enlargement, other symptoms were negative. After a few days the cough increased, dyspnœa set in, and a pleural effusion was perceptible, which in turns increased and decreased. Accompanied by high remittent fever there appeared cardiac symptoms, first on the left, and then on the right side also. The expectoration was viscid, frothy, always sanguineous, and in consequence reddish-brown (never green or purulent), and always had a peculiar faint odour. Microscopically it exhibited numerous elastic fibres, but never tubercle bacilli. As in pulmonary tuberculosis night-sweats were present ; in other respects the patients, not afflicted by heredity, had the appearance rather of malarial-cachectic persons than of consumptives. In the first

cases, in which Martin had not recognised the malarial nature of the illness, death mostly ensued after three or four weeks.   The last three patients were sent to Europe as soon as the first lung symptoms set in and recovered, one of them in spite of a previous operation for empyema. Schüffner, who is at present the medical man in Deli, is very sceptical as to this form of malaria, as in one year he made about fifteen *post-mortem* examinations on cases of tuberculosis, and saw at least an equal number of surgical cases.   The existence of tuberculosis in Deli (as communicated by letter) is also confirmed by Maurer and Zellweger.

De Brun reports from Syria (Beyrout) a *benign pulmonary affection* determined by chronic malarial infection.   It mostly affects children and young persons, especially women, and is localised in one or both *apices of the lungs* (*Pneumo-paludisme du sommet*) and is attended by a more or less violent cough, which sometimes only occurs during the attacks of fever and is mostly dry, more rarely accompanied by mucous, and sometimes by sanguineous expectoration ; the cough may be absent in some cases, but there is diminished resonance, bronchial breathing, no rhonchus (except when complications with bronchitis are present), increased vocal fremitus, and bronchophony.   In recent cases, in which it is only a question of engorgement of the lung tissue, these symptoms vanish quickly on quinine being administered ; in cases of longer standing, in which induration of the tissue has already occurred, the symptoms only subside slowly or may remain stationary.   At the *post-mortem* examination of such a case De Brun found the following condition : The tissue of the apices of the lungs were of the colour and consistency of liver, infiltrated, containing no air; the sectional surface was smooth and exuded a bloody fluid ; the bronchi and pleuræ were normal ; on microscopical examination, the alveolar walls were found to be thickened and infiltrated with embryonic and fusiform cells which, transformed in places into fibrous tissue, had obliterated the alveolar recesses and filled them with miliary fatty masses, the residue of disintegrated epithelium ; no tubercle bacilli were found.   Lègues, in Marseilles, observed a similar case of a sailor hailing from Crete. The blood as well as the expectoration contained malaria parasites ; the expectoration, however, contained no tubercle bacilli.   At the *post-mortem* examination only hyperæmia and œdema of the lungs and fresh pleurisy were found, and microscopically a very slight epithelial desquamation and a few leucocytes containing melanin, notwithstanding the fact that during life an affection of the apex had been diagnosed.

11. *Malarial pleurisy* (febris intermittens pleuritica) occurs more rarely than pneumonic malaria.   According to Hertz it is characterised by symptoms of dry pleurisy (pains, dry cough, fremitus) which appear during the attacks of fever.

In German East Africa, according to Steudel, dry pleurisy occurs as a complication of blackwater fever.

12.   Hæmoglobinuric Malarial Fever or Blackwater Fever.

Synonyms : *Bilious fever : malaria biliosa hæmoglobinurica, Febris intermittens perniciosa hæmoglobinurica, Febris remittens hæmorrhagica, Febris biliosa ; Schwazzwasser fieber, Bilious hæmoglobinuric fever, Icterode pernicious fever, Hæmaturic remittent, Yellow remittent, Black jaundice, Hæmorrhagic malarial fever; Fièvre bilieuse hématurique, Fièvre bilieuse melanurique, Fièvre ictéro-hematurique, Fièvre ictéro-hémorrhagique, Fievre hémosphénurique, Fièvre ictéro hémosphénurique, Fièvre pernicieuse ictérique, Acces Jaune, Fièvre jaune des Créoles ou des acclimatés, Fièvre bilieuss grave, Fièvre rémittente bilieuse.*

Blackwater fever, so-called by the symptom most pronounced in the eyes of the laity, namely, the secretion of blackish-red urine, has lately been the subject of numerous publications.   According to these it would appear that the geographical region of distribution of the disease is a fairly large one (see chart I.).   Its principal distribution, however, is found along the flat coasts of tropical Africa, on the west as well as on the east coast.   It is by no means a new illness in these regions, though of late years it has increased in frequency.   In the reports of the French Colonial medical officers it can be traced to the twenties of the nineteenth century.   It occurs in Nossi-Bé, Madagascar, and Mauritius, in Asia Minor (Smyrna and vicinity), Siam, Cochin-China ; while in India it only

occurs in a few particularly notorious malaria centres of Assam and Upper Burmah, as also in the Terai, at the foot of the Himalayas, which has an unenviable notoriety in consequence of the uncommon malignancy of its malarial fevers (F. Plehn). It occurs in isolated cases in Java (particularly in Pulu Bras, Onrust, in Tjilatjap and Tandjok Priok) in Atjeh and in New Guinea. A fever with the same signs and symptoms is also met with in the Southern States of North America, in the West Indian Islands, where it frequently is confused with yellow fever, in Central America, Venezuela, Guiana, in a few districts of Brazil, and in Uruguay (Montevideo). It has also been observed in Europe in a few river valleys of Spain, in some parts of Italy, especially in Sicily, Sardinia, in the Roman Campagna, as also in Greece where, during the construction of the canal in Corinth it wrought great havoc amongst the labourers.

Blackwater fever is by most authors reckoned as a variety of malaria, and in this opinion I coincide. It appears in the most notoriously malarial regions, and skilled observers such as Van der Scheer, F. Plehn, A. Plehn, Powell, &c., have found the small, unpigmented, seal-shaped malaria parasites peculiar to the tropical forms of malaria in the blood of blackwater fever patients, in most if not in every case. The large tertian and quartan parasites have also been observed a few times (by A. Plehn, Koch, Smith, &c.). Opinions deviating from the above are expressed by Yersin, Sambon and Koch. Yersin,[1] in two cases observed in Madagascar, found no malaria parasites, but discovered a fine bacillus, which he was able to cultivate on gelatine and which had a toxic effect on rabbits and mice ; he therefore came to the conclusion that blackwater fever had nothing to do with malaria. There has, however, been no confirmation whatever of this discovery. Sambon, withou however, being able to support his views by means of his own investigations, is of opinion that blackwater fever is a specific disease, which is identical with, or nearly related to, the Texas fever of cattle (see page 110). Koch quotes forty-one cases, of which only eighteen exhibited malaria parasites. On these and the following further grounds, Koch is of opinion that this disease does not appertain to the group of malaria fevers. When malaria parasites are present, their number is not proportionate to the hæmoglobinuria, as would be expected by analogy with Texas fever. In malaria the parasites are very numerous without hæmoglobinuria being originated, and on minute comparison between attacks of malaria and those of blackwater fever it will be found that essential clinical differences are exhibited. Finally, judging by the fact that blackwater fever may be connected with two entirely different kinds of malaria, namely, ordinary tertian fever and tropical fever, Koch comes to the conclusion that this disease is not related to malaria. Koch's investigations stand in direct opposition to those of F. Plehn. This investigator, who has had a wide experience in the sphere of the ætiology of malaria, states the following facts in his recently published work, " The Cameroon Coast." In the medical history of 40 cases of blackwater fever observed by him in Cameroon and German East Africa, statements were given as to the result of the examination of blood for malaria parasites in 32 of these cases. In 21 the results were positive, in 11 negative. Apart from the conditions that obtained before the appearance of blackwater fever or after its disappearance, the results of the examination were as follows :—

[1] Société de Biologie, Meeting on June 8, 1895.

			Number of Patients.			
Day of Disease.			Positive.			Negative.
First	...	...	16	...	...	3
Second	...	...	2	...	...	7
Third	...	...	—	...	...	4
Fourth	...	...	—	...	...	1
Fifth	...	...	—	...	...	1

Taking these numbers into consideration, and in spite of Koch's weighty authority as to the question of the relation of blackwater fever to malaria, I do not consider his verdict to be conclusive.

A. Plehn has pointed out that in this disease the malaria parasites are only to be encountered *at the beginning of the illness* as, in all cases without exception, these parasites perish in the plasma by being deprived of their host through the disintegration of the blood corpuscles which takes place in blackwater fever ; in consequence, malaria parasites may disappear entirely after only twelve hours. As regards the *influence of the seasons* on the occurrence of the disease, it is especially towards the end of the rainy season in most tropical countries that cases of illness make their appearance. Coinciding with this statement Bérenger-Férand reports the same condition in Gorée, Carmouze in the French Soudan, F. Plehn in Cameroon, and Corre in the island of Nossi-Bé on the northwest coast of Madagascar. On the other hand, Hébrard asserts that blackwater fever is seen on the Ivory coast and cannot be said to be dependent on the condition of the weather ; Gärtner reports the same as regards German East Africa. Sometimes blackwater fever appears in epidemic form, and this, according to F. Plehn's opinion, is always attributable to marked climatic or telluric changes.

The disease is mostly observed in persons who have made *a long stay in a malarial region* with or even without a large number of fevers to his credit. It seldom occurs within the first six months' stay, but F. Plehn saw isolated cases in which blackwater fever broke out only a few weeks after arrival. According to Crosse the disease seldom occurs after the third year in the tropics.

The different races show a varying predisposition to blackwater fever. Europeans suffer most frequently ; negroes are seldom attacked. The Chinese coolies on the Congo and at Fernando Po, on the other hand, suffer severely. The disease likewise affects Malays (Schellong), Tonquinese (Le Ray), and Indians (Rothschuh, in Nicaragua).

Sex appears to play no part in the predisposition. It is true that blackwater fever comes under observation more rarely in women than in men ; this, however, may be accounted for by the fact that there are fewer women than men in the countries where the disease occurs, and they are less exposed to the influence of malaria than are the men. Children do not enjoy immunity. Fisch observed the disease in two children aged respectively 14 months and $2\frac{1}{2}$ years.

According to F. Plehn an *individual predisposition* to frequent attacks exists, in the same manner as malaria possesses the tendency to reappear with the same symptoms, and with affections of the same organs. This holds good also in regard to blackwater fever, and in each new attack the power of resistance is diminished. Fisch nevertheless observed patients who had gone through ten or more attacks, and, according to his experience, after having recovered from the fourth attack the immediate danger of the attacks has been overcome.

It frequently happens that blackwater fever recurs even after *depar-*

ture from the malarial region, under the influence of change of climate, different manner of living, and on the voyage home or even after arrival home. Plehn points out that under these circumstances numerous Africans from the west coast fall victims to this disease on their way, or on reaching home. Crosse and Pakes observed a case in London of a patient who had returned from Nigeria a month previously, and had there suffered severely from malaria but had never had blackwater fever.

As *incidental causes*, all weakening influences that may act as pre-disposing causes in malaria come under consideration : such are chills, bodily exertions, mental excitement, rapid change of climate (as a quick journey to a hill station, or a quick voyage home to Europe in winter) working in the sun, excesses in " Baccho et Venere," parturition, injuries, &c.

Quinine forms another and very frequent incidental cause. In the different countries the outbreak of hæmoglobinuria, or blackwater fever, has been observed by various investigators (Tomaselli, Karamitsas, Pampoukis, and Chromatianos) to immediately follow the use of quinine, even in quite small doses. Of 43 cases of blackwater fever which came under F. Plehn's observation in Cameroon, 24 positively broke out a few hours after the administration of quinine ; and of 55 cases treated by A. Plehn in the same place 48 of the attacks were directly caused by quinine. Most of the attacks set in two to four hours after the administration of quinine ; in rarer cases, probably in consequence of retarded absorption, the attack commences later, even as much as ten hours after.

For this reason Koch has made the assertion that blackwater fever, as a *rule*, is solely *quinine poisoning* without malaria taking any part in the condition. Baccelli made the same assertion in regard to malaria-hæmoglobinuria in Italy ; Koch also maintains that in those cases in which the illness had not been preceded by the use of quinine, food, drink, or other substances conveyed into the body, to which sometimes the organism exhibits a remarkable idiosyncrasy in the tropics, may exercise a similar effect on the red corpuscles as quinine itself. Koch's opinion has, however, hitherto found but few supporters, and for the following reasons :—(1) Blackwater fever only occurs in notoriously malarial regions. (2) A number of reliable observers have confirmed the presence of malaria parasites, especially at the commencement of the illness. (3) It is occasionally observed in patients who have certainly not taken quinine immediately, or even for some time previously. Quennec in the Soudan saw the only person, a doctor, who on principle took no quinine, die of blackwater fever. Carré, in Africa, also knew two persons who would not take quinine ; one of them died from malarial cachexia, the other from blackwater fever. (4) Blackwater fever is only endemic in certain malarial countries ; but in other countries where quinine is taken to as great an extent it does not exist. In India, where malaria is very frequent and occurs in all forms, and where not alone malaria, but every kind of feverish disorder is treated with large doses of quinine—daily doses of 3·0 to 5·0 being quite usual—blackwater fever is "practically unknown" (Crombie). The same condition prevails in British Guiana. In Algeria neither Laveran nor Brault ever saw a case, nor was the disease observed by De Brun in Syria, although in both the countries mentioned malaria is very prevalent and a great deal of quinine is taken. (5) The same person may at times develop blackwater fever after a small dose of quinine ; whereas a few days previously, or subsequently, he can take considerably larger doses without any injury to himself. Exceptionally the observation is made that in certain persons hæmoglobinuria is origi-

nated even by small doses of quinine. In such cases it may be a question of congenital or acquired idiosyncrasy. (6) Although the use of quinine is by no means confined to malaria, blackwater fever, with remarkably few exceptions, only occurs with malaria.

Only three such cases, two relating to typhoid patients and one to a leukæmic patient, have ever become known to me; these were observed by P. Moscato and were mentioned in response to Meuse's enquiries on the blackwater fever question. Obviously in these cases there was idiosyncrasy.

For these reasons, according to my opinion, one may conclude that malarial infection plays the principal part in the genesis of blackwater fever, and that the ætiology of this disease may probably be explained in the following manner :—

In certain particularly notorious fever regions a constant destruction of red blood corpuscles takes place under the influence of chronic malarial infection. In consequence of the continued and unusual demands which are made on the blood-forming organs these no longer grow, so that they partly yield a product weakened in its capacity for resistance. A new invasion of parasites suffices—even of the otherwise benign tertian parasites—with the virus formed by them alone, or in conjunction with another poison introduced in the system, namely, quinine (exceptionally the latter alone) to cause a wholesale destruction of red blood corpuscles, infected and non-infected, and thus to originate blackwater fever. A. Plehn explains that as, in this process of disease, the least valuable blood corpuscles perish, a large dose of quinine can be borne a few days later without exercising a deleterious influence.

In *this enormous destruction of red blood corpuscles* the danger of blackwater fever consists. The *hæmoglobin* released in great quantities is partly taken up by the kidneys and *secreted with the urine*, and partly invades the circulation of the portal vein and becomes transformed into biliary pigment in the liver. The consequence is a superfluous production of bile. As the liver is unable to completely excrete this, a portion finds its way through the lymphatic vessels into the blood, and in this manner *icterus* is originated (*Senator's cythæmolytic icterus*). Hæmoglobinuria and icterus are, therefore, the principal features of blackwater fever. The accompanying type of fever varies. Sometimes, according to A. Plehn, it is tertian, sometimes quotidian, most frequently it is of an irregular intermittent or remittent type, with only very short periods of apyrexia or remissions.

Prodromal symptoms often precede the outbreak of the disease, and are similar to those that are apt to prelude malarial fever. They consist in a sensation of indisposition lasting for several days, accompanied by lumbar pains, or pains in the region of the kidneys, a dragging in the limbs, general feeling of fatigue, loss of appetite, disinclination for work, &c. Sometimes the disease breaks out owing to some incidental cause, sometimes spontaneously during the course of a simple uncomplicated malarial fever, or sometimes under the influence of certain external causes.

Fisch, in many cases on the Gold Coast, observed that the disease was preceded by fevers of an unimportant character setting in every week, or more rarely every fortnight.

The actual commencement of blackwater fever is usually characterised by a severe rigor, sometimes persisting several hours; the temperature mostly rises rapidly and soon attains to 40° or more. Cases, however, occur in which 38° is either not exceeded, or only by a few points, or

it may even run an afebrile course (F. Plehn). The patients complain of a severe sensation of oppression in the chest, and are tormented by restlessness and great terror. There is great feebleness from the very commencement and the patients are possessed by overwhelming low-spiritedness and hopelessness. The hot stage usually only lasts a few hours. The period of perspiration is also quite short and generally there is no intermission but only a remission of the fever, which is soon followed by a second rigor, and in serious cases by a third within twenty-four hours.

At the commencement of the illness violent and frequent attacks of bilious vomiting set in, accompanied by abdominal pain, so that all the drink taken by the patients to quench their raging thirst is generally vomited. Diarrhœa may also set in; the stools are always bilious, and in rare cases assume a blackish-brown tar-like consistency, in consequence of the infiltration of hæmoglobinuric serum into the intestine (F. Plehn); similar masses may also be vomited (Fisch). In other cases there is constipation at the commencement. The *liver* is frequently *enlarged* and painful, or pain is elicited by pressure, particularly in the region of the gall bladder. *Enlargement of the spleen* is still more frequent, but this may be absent or unnoticed in consequence of severe flatulence.

Icterus sets in within the first twenty-four hours. In serious cases it increases rapidly, so that after a few hours the patients are of a deep citron-yellow colour. Mostly, however, it is not very severe, and disappears again in a few days, being replaced by a complexion of a livid hue.

The *urine*, sometimes even before the outbreak of the fever, exhibits hæmoglobinuric contents, and according to the degree of hæmoglobin its colour is like claret, coffee, porter or sherry, or of a blackish-brown hue. It is opaque, and the froth made by shaking it is generally distinctly red or yellow. If allowed to stand a plentiful sediment forms which, microscopically examined, is found to contain vesical epithelium, kidney epithelium, grains and flakes of hæmoglobin, a few hæmatoidin crystals, hyaline or granular epithelium and hæmoglobinuric cylindrical casts. In addition to these there are occasionally seen granular cells, small masses of detritus, and quite exceptionally isolated red blood corpuscles.

The reaction of the urine is mostly slightly acid, it may, however, be neutral or even alkaline. The specific gravity, according to F. Plehn, is considerably increased in serious cases (1030-1032), but in milder cases is normal. A. Plehn, on the other hand, calls attention to the extraordinary lowness of the specific gravity when the quantity of organic material is taken into account. The albumen, computed according to Esbach's method, varies between ·05 and ·2 per cent. Heller's blood test always exhibits positive results spectroscopically; and oxyhæmoglobin or methæmoglobin, as also urobilin can always be confirmed in the blood (Berthier). Biliary pigment is not a constant constituent of the urine in blackwater fever, but has been confirmed in a number of cases by several observers (Bérenger-Féraud and Trouette, Kohlstock, Berthier, F. Plehn, A. Plehn). The presence of bile acid has likewise been successfully established (Bérenger-Féraud, and Trouette, F. Plehn).

The evacuation of urine is frequent and painful in consequence of the irritation exercised on the mucous membranes of the bladder and urethra by its pathological constituents. The quantity is usually diminished, and complete anuria may set in. Corré observed priapism in a few cases.

Louvet, in one case of blackwater fever, confirmed the presence of *indican* in the urine.

Anæmia of a high degree is always extant. The hæmoglobinuric contents were found by Plehn to be reduced to 40 or 60 per cent. On microscopical examination, this investigator found numerous macrocytes and so-called Ponfick's shadows, less numerous microcytes and poichylocytes and blood corpuscles always containing nuclei ; these are signs of commencing regeneration. On the other hand, no pigmentary materials were found, and the serum, in the most serious cases, proved to be slightly reddened by dissolved hæmoglobin.

Sambon observed pronounced leucocytosis, which commenced with the attack and out-lasted it a long time.

Berthier, who in two cases could only spectroscopically confirm oxyhæmoglobin in the blood-serum, and found that the colour of the latter did not differ from the normal, does not attribute the hæmoglobinuria to hæmoglobinæmia. According to his opinion, the hæmoglobin in the urine originates from hæmorrhages in the kidneys (see pathological anatomy) while the icterus is the result of polycholia.

The bodily strength of the patients rapidly diminishes, and they become emaciated in a few days. The pulse becomes small, irregular and very frequent, the heart sounds are unnaturally loud, and violent attacks of dyspnœa set in, which (as also the paræsthesia and hyperæsthesia, consisting in itching and a feeling of numbness in the fingers and toes) may be attributed to the advanced anæmia. Sometimes, also, *hæmorrhages* from the nose, gums, in the skin, &c., are observed. Frequently, in consequence of the defective activity of the kidneys, cerebral symptoms, severe headaches, somnolence, delirium, unconsciousness, set in and death may ensue from *uræmia*.

In other cases the patients die in consequence of cardiac insufficiency, formation of thrombus in the heart, embolism (F. Plehn), or through the enormous disintegration of red blood corpuscles and the serious disturbance of the process of life (Koch) connected therewith.

Death generally takes place in the second week of disease, frequently even earlier.

In a favourable case of blackwater fever the icterus and hæmoglobinuria disappear rapidly, but the urine remains albuminous for days and weeks, the irritation of the pathological secretion having caused nephritis. Indeed the patients only recover very slowly, the blood corpuscles destroyed being only replaced gradually. Often the temperature at the commencement of convalescence is subnormal. After recovery from blackwater fever the patients not rarely remain free from malaria for weeks or even months without taking quinine.

In the mildest cases of blackwater fever only one or more attacks of fever lasting a few hours occur with the hæmoglobinuria.

The *percentage* of *mortality* is given differently by different authors ; it is therefore evident that it varies according to time and place. According to Michel's observations (N. America) the mortality averages 33-50 per cent. ; according to Reynalds (Gold Coast) 50 per cent. ; according to Schellong (Kaiser-Wilhelms-Land) 42 per cent. ; according to Carmouze (India) 33 per cent. ; according to Cassan (Gorée) 32 per cent. ; according to Guiol (Madagascar) 31·6 per cent. ; according to Corré (Nossi-Bé) 28 per cent. ; according to Barthelemy-Benoil (Senegal) 25 per cent. ; according to Bérenger-Féraud (Senegal) 23-24 per cent. ; according to Kanellis (Greece) 22 per cent. ; according to Koch (German E. Africa) 21 per cent. ; according to Crosse (Nigeria) about 20 per cent. ; according to Steudel (German E. Africa) 16-17 per cent. ; according to F. Plehn (Cameroon) a little over 10 per cent. ; according to Pampoukis (Greece) 6·6 per cent. ; according to O'Neill (Madagascar) 4 per cent.

Fisch (Gold Coast) asserts that blackwater fever has become much more frequent during recent years than it was ten or twenty years ago, but that it has assumed a more benign character ; about twenty years ago, almost all the patients succumbed, whereas at the present time only about 20 per cent. die.

Fisch distinguishes two forms of the disease : the *uncomplicated* without, and the *complicated* with, obstruction of the renal tubules, with hæmoglobin and anuria, or as a consequence oliguria and albuminuria after the disappearance of the hæmoglobinuria. In the first form the termination is favourable, in the latter fatal.

Conolly differentiates three types : (1) the *sthenic*, consisting only of an attack of fever, with merely slight icterus ; (2) the *insidious*, with moderate remittent fever (not above 39°) and icterus gradually setting in ; (3) the *pernicious*, with repeated rigors, severe icterus setting in early and suppression of the secretion of urine. The two last mentioned types are usually fatal.

Döring regards as a *subdivision* of blackwater fever those cases of illness " in which disintegration of the red blood corpuscles occurs, but in which the hæmoglobin does not appear as such in the urine (hæmoglobinuria), but is first *transformed into biliary pigment* in the liver and appears as such in the urine." In three cases he saw biliary pigment ensue as a consequence of the effect of quinine on active malaria parasites. All the symptoms, with this difference, coincided with blackwater fever. In the course of the disease hæmoglobin may appear in the urine instead of the biliary pigment.

Hertz differentiates fièvre bilieuse hématurique and icteric intermittent fever (intermittens perniciosa icterica) as special forms. These are, however, undoubtedly identical.

(13) *The rheumatic hæmorrhagic form* observed by Heinemann, in Vera Cruz (Mexico), in which, after the attack, there are hæmorrhages into the joints, subcutaneous tissue, and bleeding from the nose and intestines.

4. Masked Forms.

The masked forms of malaria are characterised by a remarkable diversity. There is hardly a known disorder which malaria may not incidentally simulate. The form of the mask depends largely on individual conditions, any irritated or weakened organ or part becoming the seat of trouble. The masked forms run sometimes a quite afebrile course ; sometimes they are accompanied by more or less pronounced symptoms of fever. Splenic enlargement is not always present. Like the malarial fevers they often possess the peculiarity of appearing periodically and at regular intervals. Frequently an attack of masked malaria sets in instead of the expected fever, or on the other hand the mask, so to say, is thrown off and a veritable attack of fever develops.

Our knowledge of the malarial counterfeits are to a great extent founded on old observations. Hitherto but few blood examinations have been undertaken in this direction. If malaria exists primarily, the presence of malaria parasites in the blood will be the criterion—and this to stand good for the masked forms as well as all the others—and the extent of these obscure ailments will be found to be considerably decreased.

Triantaphyllides' opinions differ from the above : Apart from the disorders which are directly due to the presence of malaria parasites, and the organic changes left by them in the body, he considers that a *malarial diathesis*, a peculiar pathological predisposition, furnished by the parasites but not connected with perceptible organic changes, exists, which may be present without previous attacks of fever, or the patients exhibiting the signs of paludism. He attributes masked malaria to this diathesis and thus explains the absence of parasites in these ailments.

The masked forms are generally rare. It is a peculiar fact that very few statements as to their occurrence are forthcoming from the worst tropical fever regions. In certain districts, on the other hand, they are observed relatively often. During recent years, in particular, a few interesting observations from the Caucasus have been published, and these are the more valuable that their parasitic nature was verified. Zakhariane observed in the place mentioned 148 cases of malaria amongst a total of 320 soldiers, of these 27 (18 per cent.), were masked, and in them large as well as small parasites were found to be the cause (Mannaberg).

According to the present standpoint of our knowledge the following groups of masked attacks may be differentiated :—

(1) *Neuralgic* affections are the most frequent. They mostly occur in paroxysms, but do not usually exhibit a regular type. In other cases they appear continuously with marked remissions. Sometimes they are accompanied by herpes zoster (Rosenthal). Most frequently neuralgia of the fifth cranial nerve is observed, particularly supra-orbital neuralgia, accompanied sometimes by redness of the corresponding eye, increased secretion of tears and photophobia. More rarely one observes occipital or intercostal neuralgia, unilateral abdominal pain (neuralgia lumbo-abdominalis), &c., occasionally hemicrania, neuralgia of the pharynx, otalgia, neuralgia of the phrenic accompanied by dyspnœa and cyanosis in consequence of the hindered diaphragmatic respiration, are met with. Cardialgia, colic, nephralgia, testicular neuralgia, ovarian aching, coccy-dynia, pruritus vulvæ, have been recorded.

By some authors "*dry colic*" is attributed to malaria. It is frequently observed on French men-of-war cruising in tropical waters. It is called *dry-belly ache* or *bilious colic* by American doctors and is characterised by exceedingly severe attacks of colic with obstinate constipation and bilious vomiting, occasionally accompanied by jaundice. It has, as a matter of fact, however, nothing to do with malaria, and according to Hirsch's[1] investigations, is nothing but *lead colic* originated by wine or rum containing lead, drinking water conveyed through leaden pipes, utensils made partly of lead, &c.

Most of the cases of *endemic colic* observed on the Congo are, according to Meuse, attributable to anchylostomiasis.

(2) *Convulsive* seizures constitute another group. They consist of twitchings, convulsions, cramps in the calves of the legs, spasms of the glottis, sneezing, coughing, which in children is similar to whooping cough, hiccoughing, eructation, expulsion of wind, dysuria, &c.

(3) *Anæsthesia*, and such disorders as periodical amblyopia (without any apparent ophthalmoscopic lesion), hemeralopia, deafness and anosmia.

The transient *disorders of vision* without apparent ophthalmoscopic lesion, and which rapidly disappear under quinine, are, according to Guarnieri, caused by a mechanical disturbance of the circulation of the blood in the retina and choroid, due to globular stasis with consecutive œdema, particularly in the dilated veins and capil-laries. These are considered to be direct consequences of the presence of the red blood corpuscles by malaria parasites, and the engorgement of the smallest vessels by partly degenerated, necrotic leucocytes, which are almost exclusively mononuclear.

(4) *Paralyses* of varied character.

(5) *Other disorders of the nervous system*, such as asthma, angina pectoris, attacks of giddiness, sleeplessness, delirium, attacks of terror, maniacal attacks, attacks of insanity, melancholia, lethargy, aphasia, are also associated affections.

(6) *Hyperæmia* and *inflammations*, such as " colds in the. head,"

[1] *Handb. der Hist. geog. Pathol.*, Edit. ii., p. 184.

pharyngeal catarrhs, bronchial catarrhs, swellings of the tonsils and thyroid gland, diarrhœa, the vomiting of the stomachic and intestinal contents, icterus, purulent urethritis (Weber), otitis media, conjunctivitis, iritis and ophthalmia (leading to atrophy of the eyeball when of long-lasting), and skin eruptions.

(7) *Hæmorrhages* from the nose, mouth, stomach, intestines, lungs, kidneys, uterus, and beneath the skin. Porter observed a hæmorrhage in a stump after amputation.

(8) *Œdema*, partial and universal, also hydrothorax and localised pulmonary œdema (Triantaphyllides).

The diagnosis of masked malaria is grounded on the more or less periodical character peculiar to all these phenomena, as also their relation to treatment by quinine. Yet experience teaches us that neither of these are absolutely reliable signs. In fact the following affections, which lately have also been attributed to malarial infection, and to which attention has only lately been directed, are contradictory to this belief.

(9) Bodnar, Ruber, Martin and others have observed *inflammation* of *lymphatic glands*, which appear in persons who have formerly suffered from malaria, or exhibit more or less pronounced cachexia. The glandular enlargements appear partly as accompanying symptoms of intermittent fever, partly as independent diseases running their course with remittent fever. They may develop on the most different parts of the body, but most frequently affect the groin glands. They often lead to considerable enlargements, are not very painful and generally heal quickly under suitable treatment with or without suppuration. The malarial nature of inflammation of lymphatic glands appears doubtful. Probably they appertain to *climatic buboes*, to be discussed later on.

It also appears dubious if the form of lymphangitis described by Bouvel-Roncière and others [1] as occurring in Rio Janeiro and other places in Brazil, and there known as *erysipelas* of Rio de Janeiro, appertains to malaria, as asserted by this author. In this disorder the superficial or deep-seated lymphatic vessels are attacked to a greater or less extent, causing a train of symptoms resembling erysipelas. In mild cases involution and recovery occur in a short time, in others serious general symptoms set in and death may ensue in consequence of adynamia, suppuration or pyæmia. Gangrene also may be set up, or the disease may assume a chronic condition, which after a variable period may subside. The spleen is usually normal, although sometimes slightly enlarged. Often the point of departure of the disease is occasioned by scratches, &c. This is particularly the case as regards white creoles, but also occurs in negroes. Children are only exceptionally attacked, the age between 20 and 50 years is most liable. Torrès Homem attributes the disease to the exhalations from the badly laid sewers in Rio de Janeiro, as it was only after they were laid that the number of these illnesses increased. Manson attributes the severe forms of erysipelas occurring in Brazil to filaria sanguinis hominis.

(10) Martin (Sumatra) and Dempwolff (New Guinea) observed *infiltrations in the muscles of the extremities*, which appeared during remittent fever attacks and led to very sensitive fluctuating swellings, which were always curable under suitable treatment. Martin conjectures the cause of these may be vascular obstruction in consequence of flakes of melanin.

(11) Charvot, Magnani, Berthelon, Martin, Planté, &c., observed that persons who had formerly suffered from malaria, or who already exhibited signs of cachexia, suffered from *inflammation of the testicles and epididymis*, which developed without previous injury, and without a trace of acute or chronic gonorrhœa being present. Under the symptoms of remittent

[1] "*Les lymphangitis primitive de Rio de Janeiro*," *Arch. de med.*, November, 1873, May, p. 355.—Roux III., p. 13.

fever the testicles and epididymis enlarge equally and frequently cannot be isolated one from the other, while simultaneously there is some effusion into the tunica vaginalis. The pain and fever quickly disappear on administration of quinine, while the swelling requires a longer time (three to four weeks) to abate. Without quinine suppuration may set in. Not rarely atrophy of the testicle or thickening of the epididymis is left, and hydrocele persists. In the German navy also (East Asia, Africa) this affection has been frequently observed. Ziemann, in Cameroon, saw a mild case with parasites in the blood; and this observer is of opinion that the sporulation of the parasites of tropical malaria takes place in the internal organs, because perhaps the infected blood corpuscles, having suffered certain changes, are retained in the capillary network; he is inclined to attribute orchitis also to this purely mechanical influence. Fayrer reports that in India, under the influence of malaria, hydrocele frequently develops.

The affection known in the East Indies under the name of *burning of feet*, is by some authors classed with malaria, by some with beri-beri; according to my opinion, however, it appertains to neither disease. It has hitherto been observed in Burmah, Siam, the provinces of Tenasserim, in Penang and in Singapore. It is characterised by burning and spasmodic pains in the feet, especially the soles, which are so severe that the patients cannot bear the lightest covering over them, are deprived of all rest, and in consequence become much run down. Neither abnormal redness, a trace of œdema, nor painful points on pressure are present. Occasionally also the hands, or both the hands and feet are attacked; frequently there are simultaneously similar pains in the tibia. Diarrhœa and necrosis of the cornea are sometimes encountered as accompanying symptoms. The disease is difficult to treat, recovery very seldom takes place. Rasch, however, achieved a successful recovery in seven weeks in a case in Siam, which he treated with phenacetin and quinine.

5. Malarial Anæmia and Cachexia.

(Cachexie paludéenne.)

A *primary* and a *secondary* malarial anæmia and cachexia are differentiated. The latter is developed in consequence of acute, frequently repeated attacks of malaria. Exceptionally it may set in after the first attacks of fever, when it may cause death in a few weeks. The severity and the number of previous attacks are of less importance in the development of cachexia than the constitution of the patients and the hygienic conditions under which they live. In children cachexia is apt to set in quickly.

What would appear to be primary malarial anæmia and cachexia, occurring without definite attacks of fever, is a very insidious affection. In many fever-regions the whole population bears the stamp of cachexia, which occasionally develops in such localities without a distinct attack of fever having been present; the cachectic state may, though very rarely, end in death without fever having been present during the entire course of the disease.

The features of the illness in both forms are the same, and the illness may have been caused by the parasites of malignant tertian fever, or, though less frequently, by parasites of other kinds. The patients attain a pale, yellowish-green, clay-coloured, or later an ashen-grey appearance, which is most pronounced on the face and the backs of the hands, particularly at the joints (De Brun). The patients become very thin and weak, and are incapable of doing any active work. They perspire profusely, sleep badly, or on the contrary exhibit marked sleepiness,

occasionally even actual stupor. They are low spirited or of changeful temper, and exhibit a remarkable nervous irritability, which is manifested particularly in their personal sensitiveness. Sometimes during the further course of the disease, however, absolute indifference sets in. The complaints of the patients are manifold and consist of giddiness, tinnitus aurium, muscæ volitantes, disorders of accommodation, pains in the back and limbs, difficulty of breathing, cardiac palpitation and oppression in the region of the stomach. The appetite is disordered, or loss of appetite alternates with morbid hunger ; diarrhœa is often present, and icterus occasionally. Usually, but not always, there is a splenic enlargement which is usually very extensive. The spleen in recent cases is also occasionally sensitive to pressure ; it is apt to be accompanied by a sensation of pressure or pricking. The *liver* also is frequently considerably *enlarged* and sensitive.

Malarial melanodermia may also appear in the form of roundish spots of a blackish-brown colour and varying size ; they appear on the trunk and limbs during the attacks of fever and are originally of a red colour.

Craster[1] gives the name "*malarial* hand " to a peculiar pink tinge of the skin on the thenar, hypothenar and flexor aspect of the last joint of the fingers. He observed this in persons who had been in the Niger Protectorate (West Africa) more than two years ; Grant,[2] with justice, denies its connection with malaria. He, himself, in India, frequently observed a relaxation of the blood-vessels of the skin in Europeans, so that when a finger or pencil is passed over the skin, a red streak appears and remains visible a long time ; this is evidently a vasomotor appearance, which is analogous to Trousseau's tache cérébrale.

During the further course of the disease the patients become still weaker, and the anæmia is gradually transformed into cachexia. *Dropsy* sets in, and also *albuminuria ;* the latter in consequence of chronic parenchymatous nephritis. Hæmorrhages may prevail—subcutaneous hæmorrhage, and more rarely bleeding from the female genitals, the stomach and intestine have been recorded. Occasionally a scorbutic condition of the gums occurs.

In women, miscarriages often take place. According to Weatherly's observations in Africa, Florida and India, two births at term take place to one miscarriage ; this condition being attributable locally to malaria. The danger of this interruption to pregnancy increases according to the number of months pregnancy has lasted (Goth). Sterility, according to Weatherly, is also a frequent consequence of malaria.

In male persons who from early childhood have been exposed to severe malarial influences, Borelli observed, besides general retarded physical and mental development, a *stunted condition of the sexual organs ;* absence of pubic hair, a small penis incapable of erection, gave the genitals of adults the appearance of those of a boy eight or nine years of age.

In patients very much reduced in strength, *necrosis of the cornea* may occur, which in the course of twenty-four hours may lead to the total loss of both corneæ (*keratomalacia ex malaria*). This affection, according to Martin's experience, is so malignant, that the partial preservation of the power of vision can only be hoped for in young and strong persons by means of quinine and local treatment. Should only one eye at first become affected, its immediate enucleation may succeed in arresting the commencing process in the other, or lead to a more favourable course. Van der Burg and Martin advise that in every corneal affection in the tropics accompanied by fever, quinine should be given.

[1] *Lancet*, 1897, September 4, p. 621.
[2] *Ind. Med. Gaz.*, 1898, February, p. 847.

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Zellweger (in a written statement) doubts the specific nature of this affection. In Europe keratomalacia also occurs as a concomitant in diarrhœa, typhoid, and other diseases, without being considered to be caused by the direct influence of the virus of the disease on the tissue of the cornea. When a patient with fever lies motionless for days with his eyes open, necrosis of the cornea may readily occur. Zellweger, in Deli, was always able to arrest such cases by immediately ordering a highly nutritive diet, and applying a protective bandage; he did not use quinine and never resorted to enucleation.

Kipp's *keratitis dendritica* and *keratitus profunda* are two additional corneal ailments that are observed in malaria.

The former begins in the course of or after an attack of fever with photophobia, flow of tears, supra-orbital neuralgia, and a narrow superficial serpiginous ulcer resembling a skeleton leaf with lateral processes, forms on the cornea. According to Noges anæsthesia of the cornea and great sensitiveness of the supra-orbital nerve, on pressure, prevails. Under specific treatment recovery quickly sets in. The same affection is also observed in influenza.

Keratitis profunda sometimes comes under observation in malarial cachexia. A greyish infiltration in the middle or deeper layers of the cornea may slowly form. The treatment should consist in quinine, atropine and fomentations.

Other *eye diseases* may also develop under the influence of malarial infection. These are caused by disturbances of the circulation originated by red and pigmented white blood corpuscles containing parasites. Poncet, Sulcet, Yarr, &c., observed optic neuritis with peri-papillary œdema, concluding, in severe cases, with papillary melanosis and frequently with partial atrophy; they also observed retinal hæmorrhage, retino-choroiditis, diffuse opacity of the vitreous, and sudden, incurable blindness.

In *optic neuritis* supra-orbital pain and photophobia almost constantly prevail at the commencement of the disease. Night blindness is frequent, while the acuteness of vision changes conspicuously in the course of the disease. The papilla is enlarged, of a greyish-red colour, and with œdema in its vicinity; the edges of the papilla are obliterated and the vessels dilated and serpiginous. The affection is always bilateral, but as a rule does not begin simultaneously in both eyes. Almost 80 per cent. of the cases, according to Yarr, terminate in partial atrophy in consequence of endarteritis.

Retinal hæmorrhages occur in two forms, as small peripheral hæmorrhages situated in the ciliary ring, and which frequently set in during acute attacks of fever; and larger hæmorrhages in and around the papilla occurring in malarial cachexia.

Yarr describes the *retino-choroiditis* as follows : " In about 20 per cent. of the cases of acute intermittent fevers, the patients, usually towards the end of the stage of fever, complain of pain in the supra-orbital region, sensitiveness of the eyes on pressure, photopsia and photophobia. General hyperæmia, which is mostly venous, affects the fundus oculi. The papilla appears red, slightly swollen and surrounded by a grey veil. The retina is cloudy and appears to have a waved surface. This œdematous condition, the first stage of retino-choroiditis, again disappears without leaving a trace. Sometimes after repeated attacks and the development of cachexia the symptoms persist. Puncti-form hæmorrhages appear in the periphery and a chronic, slow progressive retino-choroiditis is formed, ending in capillary atrophy of the choroid with severe disorder of vision. The fundus oculi then appears of an almost uniform grey colour, as if sprinkled with pepper, the optic disc is pale, the vessels very thin, the vessels of the choroid are distinctly visible, almost white, with central red stripes; the layer of retinal pigment and the capillaries of the choroid are atrophied."

The *opacity of the vitreous* exhibits a characteristic white appearance in reflected light, and occasionally causes an almost total loss of power of vision ; all this may, however, in time clear up.

Yarr describes the following additional disorders. Sudden but persistent amaurosis without ophthalmoscopic changes (central lesion), periodical amaurosis (œdema, hæmor-rhages), amaurosis setting in suddenly and ending in atrophy of the optic nerve (perhaps hæmorrhage into the optic disc), persistent central scotoma (macular hæmorrhage), periodical blue vision (cause ?).

The treatment of the above-mentioned ocular disorders consists in quinine and change of climate ; in opacity of the vitreous iodide of potassium is recommended, with protection from light, local bleeding and blisters.

Gangrene may set in on various parts of the body; on the cheeks (noma), gums, female genitals, scrotum, extremities. The slightest *ulcerations of the skin* often become *phagedenic.* Rigollet also observed *phlebitis* in two cases in consequence of malaria. *Wounds* according to

Fayrer and Van der Burg heal with difficulty, so that surgical operations in malarial cachexia should be avoided, being attended by severe hæmorrhages and gangrene. Roux and Martin certainly had contradictory experience. Martin, however, in two cases observed retarded healing of *fractures ;* the formation of callus sets in late and is apt to be incomplete, and it was only after change of climate the definite consolidation of the fracture ensued.

Sometimes *multiple abscesses in the subcutaneous tissue* and *boils* develop. The former, according to Martin, are most frequent in the external auditory meatus, on the legs and thighs, and in the cellular tissue of the perinæum, frequently causing incomplete anal fistula. Luard and Piron each had a case of *myositis* which terminated in suppuration.

In much reduced patients *parotitis* is also frequently observed. Martin once observed the development of *hepatic abscess* and ulcerative *endocarditis ;* it is, however, difficult to see the connection of hepatic abscess and malaria.

Neuritis and *multiple neuritis* occur. Macnamara observed paralysis of the soft palate, and of the left ulnar nerve, besides neuro-retinitis. Multiple neuritis of a diversified character was observed by Regnault, Strachan and Highet. Glogner even attributes a portion of beri-beri symptoms to malaria. Nevertheless I consider the four cases communicated by him and in which he observed malarial fever in addition to beri-beri symptoms, and the aggravation of the former after the latter and *vice versâ*, to be complications of beri-beri with malaria.

The cases of multiple neuritis observed by Strachan in the West Indies were characterised by amblyopia, hardness of hearing, burning of the palms of the hands and the soles of the feet, followed by pigmentation, herpetic vesicles in the region of the nerve terminations, and peculiar inflammations of the eyes, nose, and mouth.

The disease, which occurred in whites as well as in negroes, mostly ended in recovery, but only after the lapse of months or even years.

According to Young *spinal pachymeningitis*, manifested by paresis or paralysis of the lower extremities, is often developed after severe and prolonged malaria.

Myelitis also, symptomatologically and probably also anatomically, of different kinds may, according to Remlinger, appear during the course of pernicious as well as intermittent fevers. Triantaphyllides observed three cases of *multiple sclerosis* in consequence of malaria, two of which recovered through specific anti-malarial treatment.

Sometimes, in consequence of malaria, *mental disorders* occur. According to Frerichs these are set up by a deposit of pigment in the cerebral cortex, whereas Pasmanik attributes them to the toxin formed by the malaria parasites, and more especially to cachexia. According to this author conditions of simple melancholia, perturbed melancholia and imbecility occur, all of which exhibit a depressing character. The prognosis is almost invariably favourable.

Judica observed *attacks of hysterical convulsions* with hemianæsthesia as a consequence of malarial cachexia, and which yielded to anti-malarial treatment.

We are indebted to Dehio's careful investigations for our knowledge on the condition of the *body temperature* in malarial cachexia. During its course intermittent or irregular attacks of fever appear occasionally, accompanied by slight temperature ; these, however, rarely set in separately, but mostly form persistent connected periods of fever. During the afebrile intervals, however, the temperature is abnormal, its course being irregular and atypical and similar to that of the feverish period.

The average daily temperatures are sometimes relatively high, sometimes far lower than in healthy persons, and exhibit abnormally large and quite irregular daily fluctuations. The maximum is generally attained at midday. The mechanism of heat regulation is therefore also disturbed during the afebrile periods, and not only are the attacks of fever checked but the irregularities of the afebrile temperature disappear rapidly with the exhibition of quinine. The absence of fever is therefore to be explained by the exhaustion of the organism which is no longer capable of causing high temperatures, yet exhibits during low temperatures the same abnormal conditions as in the feverish state. According to Dehio's experience the patients not infrequently become feverish when strength is regained. Malarial cachexia is therefore not to be regarded as a secondary disease, but as the continuation of the primary disease in an enfeebled —and therefore more weakly reacting—body.

The *subjective symptoms of fever* are, according to Van der Scheer, often very slight, so that temperatures of even 39-40 cause no feeling of illness. This is important in regard to the statement of some authors that malarial cachexia may exist without previous fever.

Malarial disease may drag on for months or even years. It can be borne longer by the natives of malarious countries than by Europeans. Transient improvements are effected with suitable treatment, but recovery can only be hoped for if the malarious region be left ; yet even this is not certain, and according to Werner traces of the disease remain during the whole life, even in the most favourable cases.

Death finally ensues from exhaustion, dropsy, diseases of the kidneys, amyloid and leucæmic conditions, or complicating diseases, sometimes also from apoplexy which, according to Griesinger, is attributable to pigmentary embolism of the cerebral vessels.

Topi is of opinion that malarial cachexia (like pernicious anæmia) is caused by *gastric lesions*. In several cases he discovered numerous malaria parasites in the most varying stages of development in the shrunken and degenerated digestive glands of the stomach and the surrounding capillaries.

It is a remarkable fact that malarial cachexia is observed with very different frequency in the worst malarious regions. In India, more particularly in the Terai, Deccan and North Ceylon, it is of very frequent occurrence ; in Africa, on the other hand, it is very rare. Neither F. Plehn in Cameroon, nor Koch in German East Africa, ever encountered a typical case of malarial cachexia.

Buchanan describes a *cachectic form of fever* occurring frequently in *Indian jails* at the end of the " unhealthy " season, and which is observed mostly in patients who have previously suffered from intermittent fever and dysentery. The disease commences either with low fever, or with high fever lasting a week and succeeded by low fever. The patient becomes weaker and thinner and appears anæmic. The sclerotic may assume a yellow tint ; the tongue is either large and relaxed, exhibiting indentations of the teeth at the edges and black pigmented spots, as are frequently observed in native Indians, or, especially during the further course of the disease, the tongue is red and raw. The gums are blackish-blue or red, swollen and ulcerated. Frequently between the upper and lower last molars, on one side or both, there is an ulcer known in India under the name of " *Crombie's molar ulcer*." The feet and regions of the joints are frequently œdematous, ascites often prevails also, and the spleen is enlarged. The patients frequently suffer from nyctalopia. When the patients become still weaker mucous diarrhœa or dysentery sets in, or gangrene of the large intestine such as is observed in chronic dysentery obtains, and mostly ends in death. In other cases the patients become thinner month by month till they finally succumb to inflammation of the lungs or sudden pulmonary œdema. Nevertheless

all cases are not hopeless. Recovery may set in if the patient be liberally fed.

To this category the disease called **Kála-azár** (black fever¹), which for the last twenty-five years has raged in the *valley of Assam* through which the Brahmapootra flows, also doubtless belongs. It was first seen in 1875 at the foot of the Garo Hill, and it spread from thence gradually to the east during the following years, keeping, however, mostly to the southern bank of the Brahmapootra. From the ravages of this disease about one fifth of the population have perished during the last fifteen or twenty years, so that entire districts have been depopulated and a portion of the land formerly cultivated lies waste.

Kála-azár, like ordinary malarial fever in Assam, generally sets in during the hot rainy season (March to October) and prevails mostly from April to August. It is to Rogers we are indebted for the last exhaustive communications on kála-azár, and according to this investigator it is characterised by intermittent and remittent fevers, more or less extensive anæmia, universal emaciation, great weakness and a considerable enlargement of the spleen and liver. These symptoms are frequently accompanied by a darkening of the skin (hence the name) and sometimes by œdema of the feet, more rarely by œdema of the face. The fever exhibits occasional intermissions, which may last a few days or weeks; during the later stages of the disease the fever is not so high as at the commencement, and in those who survive the hot rainy season, usually disappears during the cold dry season, to revive only too often in the next rainy season. *The duration* of the disease generally averages four to nine months, sometimes two years. There is seldom a fatal termination at a period under three months.

Death, according to the investigations of Dodds Price, occurs in 96 per cent. of the cases as a consequence of exhaustion or chronic diarrhœa, or, in the case of patients who have survived the rainy season, through pneumonia and other pulmonary affections in the cold season.

Rogers considers kála-azár to be a severe *form of malaria*. According to his observations, the disease, during its early stages, cannot be distinguished from ordinary malarial fevers, and in its later stages resembles ordinary malarial cachexia. It is, however, distinguished by its greater severity, causing cachexia in as many months as in malaria would take years; moreover it is characterised by its great resistance to quinine and also by the fact that it usually attacks several members of one family.

Rogers, in all stages of the disease, found the usual malarial parasites in the blood (unfortunately he does not mention the form); he did not, however, discover any other micro-organisms in the blood and organs, either during life or after death.

The pathological anatomy of kála-azár is the same as prevails in malarial cachexia. There is pigmentation of the liver, spleen, kidneys, &c. The ferruginous contents of the liver are increased, the yellow marrow of the medullary cavities is transformed into red.

The disease appears on *alluvial soil* and never extends far up the hills. In its distribution it follows the *lines of intercourse* and stops when it comes to uninhabited jungles. It is carried by persons visiting an infected place, and who have there fallen ill, to places hitherto uninfected; it there slowly spreads, first attacking the family of the first patient. The evacuation of the infected dwellings by the healthy and the erection of new dwellings is supposed to have favourable results. The disease always abates or quite disappears during the cold season only to break out anew during the next rainy season. Thus it goes on five to seven years, until all those predisposed to the disease are seized and often two-thirds of the village population have succumbed. Rogers saw one little Brahmin village —the inhabitants of which, for reasons of caste,

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¹ GILES, G. M. "The Etiology of Kála-azár." *Ind. Med. Gaz.*, xxxiii., 1898, No. 1, p. 1.

POWELL, ARTHUR. "Prevalence of certain Intestinal Parasites in India, &c." *Ibid.*, No. 12, p. 441.

ROGERS, LEONARD. "Report on an Investigation of the Epidemic of Malarial Fever in Assam, or Kála-azár." Shillong, 1897.

— "The Epidemic Malarial Fever of Assam." *Ind. Med. Gaz.*, xxxiii., 1898, No. 6, p. 210; No 7, p. 246.

— "The Epidemic Malarial Fever of Assam, successfully eradicated from tea garden lines." *Brit. Med. Journ.*, 1898, p. 28, p. 891.

— "On the Epidemic Malarial Fever of Assam, or Kála-azár." *Medico-Chirurgical Transactions*, lxxxi., 1898.

THORNHILL, HAYMAN. "A Criticism on Dr. Rogers' Report on Kála-azár." *Ind. Med. Gaz.*, xxxiii., 1898, No. 2, p. 50; No. 3, p. 86.

had no intercourse with their neighbours—unaffected by the disease although all the villages surrounding it had for years suffered from the disease. Than this there could be no more striking proof that human intercourse plays a large part in the spread of the disease.

Rogers is of opinion that kála-azár is an aggravation of ordinary malaria and that in consequence the disease has become transmissible from person to person, either direct through the air or more frequently by passage through the soil, a view which is irreconcilable with the present state of our knowledge of the ætiology of malaria. Ross, who has likewise studied the disease, asserts that only an indirect transmissibility of the disease by means of mosquitoes can take place.

Giles regards kála-azár as a *combination of malaria and anchylostomiasis*. The latter, however, is excluded as an essential factor by Rogers, who supports his opinion on comparative blood examinations which he conducted on healthy natives in Assam, on patients suffering from kála-azár, on patients with malarial cachexia in another district of Assam, on cases of anchylostomiasis, and cases of the latter complicated with malaria. He found that in kála-azár, as in malarial cachexia, the red blood corpuscles and the hæmoglobin were proportionately diminished, the white blood corpuscles were diminished absolutely as well as relatively, and the specific gravity somewhat lowered. In anchylostomiasis, on the other hand, the hæmoglobin is relatively more diminished than the red blood corpuscles, the white blood corpuscles are absolutely diminished yet relatively increased, and the specific gravity is considerably lowered. The numbers found in a combination of malaria and anchylostomiasis occupy a position between that of malarial cachexia and anchylostomiasis. That the anchylostoma parasites play no important part in kála-azár is proved by the fact that Dobson in 80 per cent. of the healthy coolies imported from various parts of India to Assam, confirmed the presence of these parasites. In 83 per cent. of the cases of kála-azár less than twenty anchylostoma were found during life, a number that has no effect on the blood of healthy natives, and in twenty-five cases with fatal courses fewer anchylostoma were discovered than in persons that had died of other diseases.

According to the published results the nature of kála-azár has not yet been completely cleared up. Even though Rogers' investigations have proved that malaria plays a great part in this disease the conjecture must not be excluded that there is the participation of another unknown factor, for there are several omissions in his report; he unfortunately observed no case from start to finish, and the statements as to the parasitic condition are defective.

Burdwan fever observed in lower Bengal between 1850-1870 is nearly related to kála-azár, and the disease known as *kola dukh* in Northern Bengal, near the Terai, is also probably related to or identical with it. Brown,[1] in kola dukh, almost always found large and small malaria parasites, and also crescents. The pigmentation of the skin is sometimes diffuse and most pronounced on the face and legs, sometimes spotty and exhibited on the knees, forearms, and face.

So-called *tropical anæmia* (anæmia intertropica) which formerly played a great part in tropical pathology is, in most cases, nothing but *malarial anæmia*. There is no anæmia caused by the tropical climate alone. The pale, more or less yellowish tinge of complexion, seen in most Europeans who have long dwelt in the tropics and yet are quite healthy, does not depend on anæmia, as has been proved by the examinations of blood made by Marestang,[2] van der Scheer,[3] Eijkman,[4] Glogner,[5] and F. Plehn,[6] in regard to the constituents of red blood corpuscles and hæmoglobin, and in regard to the specific gravity and the amount of water contained; these investigations showed no observable deviation from the normal condition as observed in Europe.

F. Plehn attributes the pale skin, which is not accompanied by a paleness of the mucous membranes, to the fact that Europeans in the tropics generally expose their skin less to the direct influence of the sun than they do at home, and take great care to avoid so doing. Persons exposed to the direct rays of the tropical sun, such as sailors, hunters, planters, exhibit the same healthy bronzing of the skin as in Europe. Eijk-

[1] Brown, E. Harold, " A Report on Kola Dukh," *Ind. Med. Gaz.*, xxxiii., 1898, No. 9, p. 324.
[2] "Hématimétrie normale de l'Européen aux pays chauds." *Arch. de méd. nav.*, 1888, No. 12.
[3] "Over tropische Anämie." *Geneesk. Tijdsch. v. Nederl.-Ind.*, xxx., 1890, Edit. 4 and 5.
[4] "Over zoo genaamde tropische anæmia." *Geneesk. Tijdsch. v. Nederl. Ind.*, xxx., 1890, 3rd edition. "Blutuntersuchungen in den Tropen." *Virch. Arch.*, cxxvi., 1898, p. 113.
[5] "Blutuntersuchungen in den Tropen." *Ibid.*, cxxviii., 1892, p. 160.
[6] "Beitrag zur Pathologie der Tropen." *Ibid.*, cxxix., 1892, p. 285.

man, on the other hand, regards the pale complexion as a local phenomenon, a consequence of the higher temperature which works on the vascular nerves, and he calls attention to the normal whiteness of the parts of the skin kept covered; this pallor in the parts of the skin covered by clothing is constant in a damp warm climate. The pallor is attributed by van der Scheer and Lehmann to there being less blood in the skin, on account of a larger quantity occupying the abdominal organs.

Chronic diarrhœa, dysentery, anchylostomiasis, &c., may, besides malaria, be considered as causes of actual anæmia occurring in the tropics.

Besides the above-mentioned pale complexion the following *deviations from what is considered normal in the temperate zone* occur in the body of Europeans dwelling in the tropics; these changes may be *attributed to the effects of the tropical climate.*

A long stay in the tropics causes a *weakening* of *muscular power;* this result may be directly gauged by the dynamometer and is most pronounced in the tropical lowlands; but is not observed in the tropical mountain regions, where the temperature is lower, the differences of temperature are greater, and where there is less moisture in the atmosphere.

The *bodily temperature*, according to F. Plehn, rises a few decimals (about 0·46) in transit from a moderate to a tropical climate, this rise corresponding generally to the atmospheric temperature. After acclimatisation, however, no rise of temperature is present when resting or doing moderate work. Between the hot dry season and the cooler rainy season there is a mean difference of 0·18° to 0·4°. In regard to the daily temperature there is no characteristic deviation in the tropics. There is seldom a considerable rise of the daily temperature during the early hours of the evening, such as is observed in Europe, but it is frequently influenced by exterior temperature, the taking of food, and bodily exertions. The regulation of heat in Europeans in the tropics is distinctly less evenly balanced than in temperate latitudes or than in the coloured natives. Apart from this, according to F. Plehn, the temperature in acclimatised Europeans is the same as in the natives, while by other authors it was found to be higher (Jousset, Crombie), by some lower (van der Burg, Däubler, Glogner, Lehmann).

The *pulse frequency*, according to F. Plehn, increases on an average about six beats per minute on transit from a temperate to a tropical climate. This increase, however, abates after a few weeks. In acclimatised Europeans the average frequency is, as in the negro, sixty-five to seventy-five beats per minute. Martin's opinion that through the tropical heat causing an increased activity of the heart and a decreased secretion of urine, and a consequent heightening of the tension in the arterial system, a slight *hypertrophy of the left ventricle* is originated, is not supported by other observers. F. Plehn, on the contrary, by means of Basch's sphygmomanometer, confirmed the fact that the pressure of blood is diminished in consequence of the dilation of the peripheral capillaries during the entire duration of the stay in the tropics.

The number of *respirations*, according to F. Plehn, rises a little on transit from the temperate to the tropical climate, to again decrease after a few weeks. In acclimatised Europeans the respirations average fourteen to seventeen per minute.

The *secretion of perspiration* in Europeans in the tropics is increased particularly in new arrivals, but decreased after years of stay there. Even the natives perspire, but not to the extent that Europeans do.

The difference between the temperature of the skin and body in Europeans is, according to Stokvis, in the tropics 1°, in Europe 4·5° to 5·5°. F. Plehn found that the temperature of the skin was 1° higher during the rainy season than during the dry season (37·4° compared to 35·8°).

The skin of Europeans becomes sensitive in the tropics, so that on slight exposure there is a tendency to take cold.

The *secretion of urine* is, according to most authors, diminished, and the specific gravity correspondingly increased. F. Plehn found that the absolute quantity of urine, though subject to considerable individual fluctuations, did not differ materially from that in the native land, yet it is relatively diminished in comparison with the great quantity of liquid imbibed, this being a consequence of the severe perspiration. The specific gravity is dependent on the quantity secreted, but it is generally higher than at home.

The existence of a kind of *climatic atrophy of the kidneys* in persons who have lived long in the tropics, is insisted on by Dundas, but is unconfirmed by other reports.

Eijkman contradicts the old opinion that the air in tropical climates contains less oxygen than in temperate climates, in consequence of the increased vapour tension, that the absorption of oxygen in the air is decreased, and that therefore the assimilation is diminished. Eijkman asserts that no essential difference is exhibited in this particular between Europeans in Europe, Europeans in India, and natives (Malays), at least when at rest and in light occupation. In tropical residents, therefore, no chemical *heat regulation* (regulation of heat production), but only a physical one (regulation of the amount of heat lost from the body) through the increased function of the skin, takes place.

According to Glogner, the *amount of heat lost by means of radiation and conduction* is greater in natives than in Europeans, while according to Eijkman there is no important difference.

The *gastro-intestinal activity* is sluggish, and there is *a tendency to constipation,* which, according to Schellong, is sufficiently explained by the quantity of fluid parted with through perspiration and the consequent rapid consolidation of the intestinal contents, and by a relaxation of the muscles of the intestines, in harmony with the relaxation of all other muscles.

Opinions do not coincide as to the quantity of blood contained in the mucous membranes of the stomach and intestines in relation to the fulness of the vessels of the skin. According to one opinion there is a certain hyperæmia, according to another a certain anæmia.

After several years' stay in the tropics, a certain *weakness* of the *large* intestine often sets in accompanied by several loose stools following each other quickly immediately on leaving the warm bed and going into the cool morning air, while during the day no other stool follows (van der Burg, Martin).

In regard to the *liver*, most authors are of opinion that Europeans soon after arriving in the tropics from a temperate climate generally develop a more or less pronounced *hyperæmia* and *enlargement of the liver*. This is at first attended by increased secretion of bile, followed later by diminished secretion of the same; it generally, however, is introduced without subjective disorders, and is regarded as the consequences of a permanently high temperature, or owing to imbibing large quantities of liquids (Treille). F. Plehn, on the other hand, considers it is not proved that the function of the liver in the tropics is changed. According to his observations in Cameroon, where hepatic ailments occur relatively frequently, he doubts that the liver is characteristically influenced by climate, and is of opinion that this organ, like the stomach, intestine, &c., only acquires a slighter power of resistance.

Puberty in Europeans sets in at an earlier age in the tropics than in temperate climates, though not so early as in the natives. The early activity of sexual functions should not, however, be grounded on social conditions in the slightest degree.

Disorders of menstruation (amenorrhœa, menorrhagia, hæmorrhages at the climacteric) are more frequent in European women and miscarriages also occur more often than in Europe. The tropical climate, however, is less to blame for this than malaria. Fertility diminishes, and, according to statements unsupported however by direct proof, is supposed to cease after two or three generations. The statement also has been made that all European women living in the tropics suffer from "whites," but Stratz has confirmed the fact that most European women have no discharge, and that in any case there is no specific tropical discharge.

The influence of the tropical climate on the nervous system is mostly manifested in *sleeplessness* and *nervous excitability*, which, particularly under the simultaneous influence of malaria, may develop into pronounced neurasthenia.

Besides the continuous high temperature and absence of the tonic effects of change of season, other desiderata come under consideration, such as annoyance at the indolence of the natives and the worries consequent upon residence in an unsettled country.

As the functions of assimilation and nutrition are decreased the *bodily weight* is also diminished.

Many disordered conditions—the blame for which is thrown on the climate—are really due to venereal excesses, the abuse of alcohol, and the too free use of tobacco.

PATHOLOGICAL ANATOMY.

The principal changes found in the cadaver in malaria are :—

(1) *Enlargement of the spleen*, which in recent cases is due to hyperæmia and infiltration of leucocytes, is in cases of longer standing owing to hyperplasia, and later on still to induration, or occasionally also to amyloid degeneration. The enlargement in chronic cases may be so considerable that the organ occupies the greater part of the abdomen. The spleen is also frequently quite soft, especially in acute cases, sometimes to such a degree that it appears as a bag filled with black, atheromatous blood. Occasionally such softened organs rupture ; this occasionally occurs spontaneously, or is caused by slight bodily exertion, or slight unimportant injuries to the abdomen, and almost invariably induces a fatal termination. In chronic

cases the spleen is firm and tense; on section it is found to contain a great deal of pigment, and the capsule is mostly thickened and adherent to the neighbouring organs.

In tropical malaria the enlargement of the spleen is not so constant as it is in endemic intermittent fever. Even in very serious tropical fevers there may be no enlargement, or to a very minor extent. Rochard, in twenty-two cases of malarial fever with a fatal termination in Madagascar, found no enlargement at the *post-mortem* examinations (F. Plehn).

Splenic infarcts becoming purulent or gangrenous are rare conditions.

(2) *Melanæmia.*—Pigment in the form of granules or flakes, black, or more rarely brown or yellowish-red, is found, partly free in the blood, partly locked up in leucocytes or vascular endothelia. Pigment is likewise found in the spleen, liver, bone-marrow, brain, spinal cord, kidneys, heart, lungs, lymphatic glands, skin, serous membranes, &c., and impart a characteristic slate-grey or chocolate-brown colour, which is principally exhibited along the course of the vessels to these organs. The pigment, by predilection, agglomerates in the capillaries of those organs in which the circulation is retarded, such as the spleen, the bone-marrow, the liver, and in the two last mentioned it also invades the tissue elements. In this manner the blood is gradually cleared of pigment (Kelsch).

The pigment exhibits great resistance to mineral acids, even when concentrated and boiling, whereas when treated with alkalies it assumes a light brown or yellow colour and is dissolved by sulphate of ammonia. Its ferruginous contents are not constant. Stieda found that it was ferruginous in the liver, and free from iron in the vessels and spleen.

As with the enlargement of the spleen, so with the melanæmia. In the severest forms of fever causing death in a short time, one frequently finds light, thin blood, entirely without pigment, and also extreme pallor of all the internal organs except, of course, the spleen, which in the majority of cases is strongly pigmented (F. Plehn).

As to the other changes in the blood, exclusive of the malaria parasites mentioned above, the number of *red blood corpuscles* is often diminished to one half, to one quarter, even to one-tenth of the normal, and their hæmoglobin constituents are decreased. The decrease of the red blood corpuscles is in proportion to the quantity of parasites. There are found, besides, megalocytes, granulated red blood corpuscles, microcytes, poichylocytes, in short, all the phenomena peculiar to severe anæmia.

As to the condition of the *white blood corpuscles*, the statements of authors do not coincide. According to Vincent's observations, there is sometimes considerable leucocytosis at the commencement of the attack of fever which, nevertheless, disappears again after from six to fifteen minutes, so that it may easily escape detection. The increase, above all, concerns the lymphocytes, and in a less degree the eosinophiles and the large single nucleated cells, and is due to an influx of cells from the spleen (lymphocytes and macrophages), lymph glands (lymphocytes), bone marrow (eosinophile cells) and liver (macrophages). The leucocytosis is followed by a hypoleucocytosis. The number of white blood corpuscles is sometimes two to three times less than before the attack, and may still decrease the day after it and then again gradually increase. The activity of the phagocytes relates almost exclusively to the single nucleated cells (micro- and macrophages) and these are, thereupon, retained in the spleen and liver in their passage through the lymph glands. In malarial cachexia the white blood corpuscles, according to Kelsch, are relatively and absolutely diminished. Babes and Gheorghin observed, on the other

hand, that in chronic afebrile malaria there is always severe leucocytosis. Grawitz found the eosinophile cells relatively increased, especially in malarial anæmia.

In *blackwater fever* punctiform and larger *hæmorrhages* were found in various organs, as in the brain, retina, pericardium, pleura, mucous membranes of the stomach and intestines, mesenteries, capsule of the kidney, kidney-pelvis and subcutaneous tissue.

The *heart* is mostly dilated and the myocardium pale, relaxed and shrunk, but not always showing fatty degeneration. Frequently there is an extensive formation of thrombi. Occasionally ecchymoses are discovered in the pericardium and endocardium.

The *lungs* are often hyperæmic and œdematous, and occasionally exhibit hæmorrhagic infarcts. In one case of malarial pneumonia I was able to confirm brownish-red and greyish-red hepatisation. In milder cases, in which the local phenomena disappear during the intermissions of fever, it may not go beyond *engorgement*.

The *mucous membrane of the stomach* frequently becomes hyperæmic, and in hæmatemesis may be ecchymosed. In *blackwater fever* Döring found it in the most advanced condition of inflammation—even hæmorrhagic in places—and covered by a very thick layer of viscid mucus, stained green by bile.

The *intestine* is likewise frequently the seat of hyperæmia and catarrh, or is ecchymosed. The solitary follicles and Peyer's patches occasionally exhibit enlargements and pigmentation. In the *choleraic malaria* condition, Marchiafava found the parasites principally localised in the small vessels of the dark red or chocolate-coloured mucous membrane of the intestinal tract, whereas the other organs contained only a few parasites or none at all. In *malaria dysenterica* the large intestine, according to Werner, exhibits round or irregularly formed ulcerations, 1 cm. or more in diameter, the base of which is formed by the opaque serous covering, and is often covered with detritus. The mucous membrane, at the same time, varies in colour from bright red to dirty violet and slate-colour; it becomes swollen and relaxed and exhibits occasionally small cicatrices, depressions and contractions. Frequently also the ileum exhibits the same condition. In *malarial typhoid*, besides deposits of pigment in various organs, the changes characteristic of typhoid are found in the intestinal canal.

The *liver* in *acute cases* is frequently enlarged, hyperæmic, dark red and soft, or, after the disappearance of the hyperæmia remains of a chocolate or slate colour. In *blackwater fever* and in cases in which all the internal organs exhibit more or less icterus, it is very deeply stained and more or less yellow.

The hepatic ducts are always patent (Fonceroines), and like the gall bladder are found to be filled with dark, greenish-black thick bile.

Conolly, in *blackwater fever*, found numerous nodes varying in size from the head of a pin to a pea, and which on incision were found to be cysts filled with a thick, fluid caseous mass of a light yellow colour.

The agglomeration of pigment in the intra-lobular spaces is sometimes so marked that the periphery of the lobes appear to be surrounded by a distinct black zone. The intra-lobular capillaries are dilated, their endothelium swollen and pigmented, and they contain malaria parasites, frequently in so great a number that they are entirely blocked. In the hepatic cells no black pigment is found, but more or less yellow pigment is present. In other respects the hepatic cells are sometimes normal, and

sometimes exhibit cloudy swelling or fatty degeneration; sometimes they are atrophic or necrotic.

In *blackwater fever* the acini often appear distinctly separated (Döring) by seemingly dilated biliary ducts filled with dark green bile.

Occasionally numerous ecchymoses are found in the liver, or scattered and confluent inflammatory and suppurative foci, which, however, have probably no connection with malaria.

In *chronic cases* the liver is mostly large and firm, in consequence of increase of connective tissue; it is much pigmented, often granular (hypertrophic cirrhosis), more rarely of normal size or shrunken as in ordinary hepatic cirrhosis; the capsule is usually thickened. Sometimes, also, amyloid degeneration is observed.

Occasionally the liver is observed to be atrophic without cirrhosis, appearing anæmic and chocolate coloured; in such cases the heart and kidneys also are usually atrophic and pigmented.

The *kidneys* in many cases are normal or they are hyperæmic or pigmented. In *blackwater fever* hæmorrhages partly sub-capsular and partly interstitial are sometimes met with, and on section the pyramids appear dark reddish-brown, and the cortical substance lighter. Pellarin and F. Plehn observed hæmorrhagic infarcts, and the former observed abscesses also in the cortex.

Microscopically, in fresh cases, the epithelium of the urinary tubules and Bowman's capsules are found to be normal; in cases of longer duration of the disease there is albuminous infiltration of the same, and the urinary tubules are obstructed with hyaline casts and yellow pigment; the pigment is more especially present in blackwater fever; there is also often an increase of the interstitial connective tissue.

In chronic cases, hypertrophy of the interstitial connective tissue, diffuse inflammations, amyloid degeneration and sometimes also cirrhosis, are observed.

In regard to the *brain*, when cerebral symptoms have previously existed, hyperæmia and œdema of the cerebral substance and of the cerebral meninges are found along with agglomerations of fluid in the ventricles and occasionally softening of the brain tissue. The cerebral vessels are, as a rule, remarkably rich in malaria parasites and sometimes small hæmorrhages are found in the vicinity of the vessels containing parasites (Thin). The cerebral cortex is often more or less pigmented, slate-grey or chocolate coloured; the same condition is met with in the grey matter of the medulla.

In the *algide form* of malaria the brain appears pale, bloodless, dry and viscid. In *blackwater fever*, also, Steudel found, besides dryness of all the organs, that the brain was so dry and small that it no longer filled the cranial cavity, the sinuses were filled with blood and the cerebral meninges were œdematous.

In one case of *malaria perniciosa comatosa* which Jancsó observed in Klausenburg, there was no obstruction of the cerebral capillaries through parasites or pigment, and he is of opinion that the serious cerebral symptoms are originated by the *toxic products of metabolism* of the parasites.

The *muscles* frequently exhibit fatty degeneration.

The bone-marrow is often dark, hyperæmic, and softened or even deliquescent. Its vessels contain parasites and pigment in great quantities and these are even found outside the vessels in the medullary tissue itself. In *malarial cachexia* the medulla of the long hollow bones is always changed into red medulla (Rogers).

DIAGNOSIS.

The diagnosis of malarial disease is especially founded on the proof of *splenic tumours, parasites in the blood,* and *melanæmia.* Parasites and pigment, however, are not always to be found in the peripheral blood. In such cases the blood for examination must be extracted from the spleen by means of a Pravaz syringe with the application of antiseptic precautions. The presence of one single parasite in the blood confirms the diagnosis (Mannaberg). The ætiological diagnosis is especially necessary when malaria appears in the course of other illnesses or injuries, and after parturition.

The *intermittent fevers* generally offer no difficulties in diagnosis. In the differential diagnosis tuberculosis, suppurative processes (hepatic abscess), pyæmia, ulcerative endocarditis, urethral fevers, attacks of fever in consequence of the passage of gall stones, and the attacks of fever occurring in filariasis, must be taken into account. Errors in diagnosis are avoided by carefully taking the temperatures, by having regard to the history of the disease, and by due attention to the accompanying symptoms.

Boisson, for diagnosis of intermittent fevers, applies the following sign observed by him and designated *signe de l'ongle.* With the commencement of the rigor the pinkish tinge of the finger nails assumes a peculiar dirty-grey slate coloured hue. This attains its height in the hot stage, and disappears gradually with the decline of the fever. This phenomenon probably has some connection with the transformation of the hæmoglobin into melanin, which takes place during an attack of fever.

It is easier to mistake remittent and continued fevers for gastric disturbance, catarrhal jaundice or typhoid, but even in these forms the expedients above mentioned should suffice for diagnosis.

In the differential diagnosis between malaria and typhoid it should be borne in mind that in malaria herpetic spots are frequently present, but except in so-called malarial typhoid a rash is never observed.

The *comatose form* may be confused with heat apoplexy, meningitis, uræmia or cerebral hæmorrhage. The absence of hyperpyrexia, stiffness of the neck, oculo-motor paralyses and albuminuria on the one hand, and the presence of fever (41-42° and more), splenic enlargement and, above all, of parasites in the blood on the other, should decide in favour of malaria. Sometimes in partly unconscious patients the sensitiveness of the spleen on pressure reveals malaria.

The *choleraic form* has a great similarity to *Asiatic cholera,* but can easily be distinguished therefrom by the blood examination and the bacteriological examination of the intestinal evacuations which, in malaria, will show no cholera bacilli.

The *dysenteric form* and *malarial pneumonia* may present greater diagnostic difficulties, but the type of fever, the presence of a splenic tumour, and the presence of malarial parasites in the blood confirm the diagnosis.

Blackwater fever may, under certain circumstances, be mistaken for yellow fever. In differentiating the two illnesses the following points should be considered : (1) the different regions of distribution ; (2) blackwater fever only attacks persons who have lived for some time in malarial districts, yellow fever, on the other hand, attacks new arrivals ; (3) the characteristic condition of the urine in blackwater fever, though in very rapid cases with a fatal termination this may escape observation on account of anuria ; (4) the appearance of jaundice in blackwater fever after

a few hours, in yellow fever only after two or three days ; (5) the presence generally of splenic tumour in blackwater fever, and its absence in yellow fever ; (6) in blackwater fever coffee ground vomit (vomito negro) is of very rare occurrence, but in yellow fever it is very frequent ; (7) adynamic symptoms are in blackwater fever observable from the commencement of the attack, whereas at the beginning of yellow fever there are symptoms of congestion (redness of the face, glistening eyes, with reddened conjunctivæ and a hot skin).

Below's statement that blackwater fever is a form of endemic yellow fever has received a satisfactory contradiction by F. Plehn.

The *masked forms* are recognised by their periodicity, their behaviour to quinine, and the presence of parasites in the blood.   In malarial regions the possibility of masked forms of malaria should never be lost sight of in dealing with atypical forms of illness.

Kohlbrugge, in doubtful cases, makes use of *mountain climbing* as a diagnostic assistance.   He causes the patients to climb mountains and then be sponged with cold water ; if no fever sets in on the following day they are not suffering from malaria but from other diseases.

PROGNOSIS.

The prognosis of malaria depends on the age, constitution, manner of life, social position of the patients, and on their length of stay in the malarious districts, also to a large extent on place, season, and the form of the disease.

Firstly, in regard to *age*, the early age of childhood and old age are the most dangerous.   According to Davidson, the highest mortality is in infants under 1 year old.   In the Teutonic race the impossibility of becoming acclimatised in the tropics is due primarily to the great mortality of children in consequence of malaria.   In the case of strong young persons recently arrived in malarious districts the prognosis, even in severe forms, is not unfavourable, while those persons who are the subjects of a diathesis, such as syphilitics, for instance, and persons who have already dwelt long in the tropics, the disease is always more serious.

Any and every excess in the manner of living and general unhygienic conditions render the prognosis unfavourable.

As regards the different forms of malaria, the prognosis, taken generally, is good in intermittent fevers, remittent fevers and masked forms ; unfavourable or doubtful in the severe remittent and pernicious fevers, more especially in the algide and choleraic forms, and in blackwater fever.   In the latter the prognosis, to a great extent, depends on the activity of the heart and kidneys.   If, after defervescence, a copious secretion of urine takes place, this is a good sign, whereas if anuria persists longer than one or two days the outlook is serious.   The prognosis is very bad when there is cardiac weakness and when thrombi form in the heart.   This symptom, according to F. Plehn, can be recognised by loud cardiac murmurs and very frequently irregular action of the heart. Moreover, early marked icterus, severe bilious vomiting, severe hæmoglobinuria, hiccough, and the setting in of cerebral symptoms, must be regarded as unfavourable signs.

Even in apparently mild cases when the illness is attended by an adynamic state, faintings or severe headaches must always awaken suspicions that the disease may take an unfavourable turn.

In *chronic malarial infection* the prognosis depends on the degree the

disease has attained.   Should the symptoms be only moderately developed, should the spleen and liver not have attained a great size or become in-durated, and should the kidneys be still healthy, hopes of recovery need not be banished.

It is difficult in various cases to prognosticate in regard to *relapses* continuing.   If a splenic tumour remain, one must always be prepared for relapses, and they may even occur without enlargement of the spleen being present.   So long as malaria parasites are in the blood, relapses may be expected.

The observation of the body weight is useful in this respect.   Accord-ing to R. Müller's experience, all patients who, in spite of good care, did not increase in weight, were liable to again have fever.

PROPHYLAXIS.

GENERAL PROPHYLAXIS demands, according to locality, the draining of swamps, the thorough and permanent drainage of land and continual culti-vation of the same, the control of rivers by damming their banks to prevent them overflowing; terracing the land; covering malarial soil with healthy soil, as was done in Rome and Wilhelmshaven with favourable results; small malaria centres should be *permanently flooded;* and in *towns, the streets and yards should be asphalted and cemented.*   Good results have been attained in various places on the surface of the globe by *planting shrubs, trees, &c., that have the quality of absorbing water.*   Such plants are the sun-flower (*helianthus annuus*), various species of eucalyptus (more especially *E. rostrata* and *E. globulus*), water-rice (*zizania aquatica*), the calmus (*acorus calamus aromaticus*), *the anacharis alsinastrum,* the banana (*musa paradisiaca*), the melon-tree (*carica papaya*), the conifer filao (*casuarina equisetifolia*), the Japanese kiri-tree (*Paulownia imperialis*).   On the German East-African coast the cocoa palm has been found of most service, while in Surinam the planting of the parwa-bush (*avicenna nitida)* has had good results.

It is, however, of still greater importance to *seek out and destroy the breeding places of mosquitoes in the vicinity of the dwellings,* but it is not, as Ross believes, easy to carry out this measure everywhere, as for instance where rice is cultivated.   The larvæ of the genus *anopheles,* which are the only larvæ of importance, may be easily recognised by the fact that they float like little rods, flat on the water.   In order to destroy the larvæ, insect powders, petroleum and aniline dyes (*larvicides*) have, according to the experiments of Celli and Casagrandi, proved the most practical and the cheapest.   General preventive measures cannot always be carried out ; more particularly is this the case in new colonies.

PERSONAL PROPHYLAXIS is therefore of much greater importance.   The greatest security is naturally afforded by *avoiding to pass over malarial soil;* this is, however, impossible to any one who is living in the tropics. When possible, however, a favourable season should be chosen for one's date of arrival, at which time malaria is at its lowest ebb.

The *question of the dwelling* is of great importance, and the principal rules to be followed in building a house in the tropics are here laid down.[1] The greatest care should above all be exercised in the choice of the build-

Compare Fisch, *Tropische Krankheiten,* Basel, 1894, p. 10 ; Däubler, *Die Grund-züge der Tropenhygiene,* München, 1895, p. 63 ; Scheube, article *Tropenhygiene, in Eulenburg's Encyklop. Jahrbb.,* viii., 1899, p. 584.

ing site.   If possible an elevated spot with a rocky subsoil accessible to
the winds and situated at a distance of 1-2 kilometres to the windward
of swamps.   The foundation should be covered to a depth of from $\frac{1}{2}$-1
metre with tightly packed gravel, or better still, should be asphalted
or cemented.   The house should be supported on a sub-structure, formed
of pillars, arched buttresses, or iron piles, and should be surrounded on
all sides, or at least on two sides, by a verandah 2 or 3 metres wide,
and the top of which is formed by the wide projecting roof; here one
may sit during the day, and can change one's position according to
the direction of the wind and the position of the sun.   The longest
frontage of the building should be so placed that the principal winds may
blow unchecked upon it, and it should be only one room deep, so that
through ventilation is possible.   Should the house have two stories, the
upper one is preferable for dwelling and more especially for sleeping in.
In order to keep out the mosquitoes, the doors and windows should
either be closed at sundown or provided with wire-gauze shutters.
Slates, or pressed and varnished palm-leaves, are to be recommended
for roofing the house.   The kitchen and the latrine (which should be on
the bucket system) should be a little distance from the house, but
connected by a covered way and situated so that the kitchen smoke and
the ventilation from the closet should not be blown into the house by
the wind.   No house should be without a bath room.   The space round
the house should be slanted away from it downwards, and be cemented
so that the rain-water flowing off the roof can be quickly conducted away.
Martin advises the digging of a trench about 1 metre deep round the
entire compound, adapted to receive the water pouring off the roof and
connected by a gutter with the nearest water course; constant care must
be taken to keep the trench clean and free of mosquito breeding places.
The trench also serves to drain the soil below the house.   As the smell of
eucalyptus trees and castor oil plants is said to keep off mosquitoes, it
might be well to plant some near the dwelling on the chance of their so
doing.   Care must be taken to ensure plenty of light and air in the
house, and cleanliness should reign supreme.   The dark corners of
the house should be scrupulously searched for mosquitoes, which are
wont to sleep there during the day.

 Clothing suitable to the climate also plays a not unimportant part in
the prophylaxis of malaria.   The clothing best adapted for the tropics is
underwear of cotton stockinette, and loose cotton upper garments, or
soft, loose white woollen stuff or flannel.   A tropical helmet made of cork
or light Indian vegetable pith is the proper head-gear.

 In regard to *food*, the opinion formerly prevalent that man in the
tropics requires less nourishment to maintain his alimentary balance than
in a temperate climate, is exploded.   By means of experiments conducted
especially by Eijkman it is proved that in order to maintain in the tropics
the same bodily condition and the same power of doing work, as much
nourishment (reckoned in calorics) is required as at home.   During the
summer heat of the tropics, however, there is less desire for meat and
fat.   In consequence, more carbohydrates are taken, the food consists of
a large proportion of vegetable matter and in its composition approaches
somewhat that of the natives of the tropics, which consists principally of
vegetables, rice, bananas or yams, &c., being the usual form.   It is
important to tempt the appetite by judicious choice of food and agreeable
variety, and to ingest the necessary quantity of nourishment in the most
digestible form possible.   In places where game cannot be obtained,
where no cattle are bred and where indigenous vegetables cannot be

cultivated as they are in high lying regions, it is advisable to follow
more or less the customs of the natives, and to reduce tinned provisions
to a minimum. I consider the mode of life generally adopted in the Dutch
Indies by Europeans worthy of imitation, the midday meal (rice meal)
consisting of indigenous food and the evening meal of European food.
Due attention, also, is paid to the necessity for a regular, but not ex-
aggerated, supply of stimulating comestibles, which according to the
opinion of experienced tropical doctors no doubt exists, and is to be ex-
plained by the fact that the anæmic mucous membrane of the stomach re-
quires stronger stimulants than in a temperate climate (see above, p. 154).
The curry taken with the Javanese meal of rice is composed of a mixture
of various spices, of which Chili pepper (capsicum annuum) is the most
important. It is certainly not by chance that all natives of tropical
countries, without respect to race or creed, make plentiful use of this
spice in their food, and assert that they could not exist without it.
Martin is of opinion that pepper may perhaps correct the tendency to
contract malaria. The Tamils, who according to his experience are most
immune, are also the greatest eaters of pepper. As for myself, personally,
during my stay in the tropics, I found nothing suited me better nor did
I enjoy anything more than rice with curry and the usual addenda of
which the Javanese meal of rice consists, and this actually became a
necessity to me. Schellong, on the other hand, is of opinion that the
idea of spices and pepper being necessary in the tropics is one of the many
customary prejudices so numerous in tropical life. In any case an
excessive use of spices in the tropics may have a deleterious effect and
may lead to chronic dyspepsia and favour the appearance of sprue (see
sprue). Fruits, so plentiful and manifold in the tropics, are also useful
when eaten in moderation, for they excite the appetite and the secretion
of the gastric juice and assist the flagging digestion. A superfluity of
fruit is, however, injurious, and may cause indigestion, diarrhœa and
dysentery, and thus indirectly induce malaria.

The provision of good *drinking water* is of great importance. Where
this is not obtainable, the water to be used should be sterilised by being
boiled for an hour, or by the addition of chemicals (chlorinated lime,
bromine, tincture of iodine[1]). Filters made of animal charcoal, asbestos,
unglazed porcelain, &c., have not proved of general value, as they require
to be cleaned very frequently to remain effective, and this is practically
difficult of accomplishment. The drinking of tea or coffee in lieu of water,
under certain circumstances, is to be recommended.

There is nothing to be urged against the moderate use of wine and
beer, and the same may be said of tobacco. Excessive indulgence in either
should be strictly avoided.

The *manner of life* should in every respect be regulated. Inactivity
is just as injurious as over-exertion. Frequent baths or cool shower
baths are recommended. One should avoid, as far as possible, everything
which, as we have seen above (p. 120), predisposes the constitution to
attacks of fever.

Expeditions, as well as necessary earth works, should, when possible,
be undertaken during the healthy season. Troops should be disembarked
during the day-time. The unhealthy regions near the coast must be rapidly
crossed by the men so that they may reach the healthier interior as soon
as possible. Night marches should be avoided equally with marches

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[1] More minute information in Scheube's article "Tropical Hygiene," in Eulenburg's
Encyklop. Jahrbb., viii., 1899, p. 584.

during the hottest hours of the day. The same applies to sleeping in the open air. If, however, it is unavoidable, the face and neck should be covered with a veil, gloves should be worn, and a fire lighted.

In order to obtain effective *protection from mosquito bites*, above all the use of a well-closed mosquito net during sleep is necessary, besides the above-mentioned precautions. For the same purpose deodorants may be used for anointing the body, such as turpentine, iodoform, menthol, nutmeg, camphor, garlic, tobacco smoke, unexpanded chrysanthemum flowers,[1] eucalyptus leaves, quassia chips, pyrethrum, or the burning of sulphur; protective measures which have been tried by Celli and Casagrandi and found effective.

In conclusion, the *prophylactic use of medicaments* have to be mentioned, and for this purpose *quinine, arsenic* and *iron* are principally recommended.

Quinine as the sovereign means of preventing malaria has the most adherents. It is given prophylactically either in daily small doses (0·15 to 0·3) or in larger but less frequent doses (0·5 every third day or 0·5 to 1·0 every five to eight days). The former method is mostly adopted by British and French doctors; the latter is particularly recommended by German doctors (A. Plehn, F. Plehn, Steudel, Koch, &c.). The German method decidedly merits the preference, because larger doses have more chance of destroying the malaria parasites that may have invaded the body. Unfortunately, quinine possesses the disadvantage that its continued use injures considerably the digestive organs, which have otherwise been already changed by climatic influence. It is therefore not advisable, when living long in a malarious district, to take quinine habitually; it should only be taken after exposing oneself to notorious malarial infection (see p. 120), or when prodromal symptoms indicating fever (see p. 122) set in; its use should be continued for several weeks. Ziemann's advice is very rational, namely, always to examine the blood of those suspected of fever, and only to administer quinine when parasites are actually found in the blood. By this method he succeeded in warding off the outbreak of fever in 50 per cent. of all cases. It is, however, only possible to adopt this proposition under certain favourable circumstances. Quinine is best borne when taken during a meal (Laveran). Others advise that quinine be taken in the evening because then the troublesome singing in the ears is slept off.

Arsenic, which does not directly influence the malaria parasites, is recommended prophylactically because it improves nutrition and in consequence increases the power of resistance of the organism. Arsenic is used chiefly in the form of Fowler's solution. Two drops daily are commenced with, the dose is increased daily by one drop up to twenty drops, and then again gradually decreased. The treatment, however, must not be continued too long. Generally, according to Martin, four to six weeks suffice for new arrivals. Favourable results have been attained with arsenic by Tommasi-Crudeli, Brunhoff, R. Müller, Martin, &c., whereas Duncan found it ineffective.

Schellong advises prophylactically the frequent use of *iron preparations* combined with quinine.

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[1] Celli especially recommends a powder consisting of unexpanded chrysanthemum blossoms, valerian roots and larvicide, which is sold by the Italian pharmacological Society in Rome under the name of "zanzolina." One tablespoonful of this suffices to stupefy the mosquitoes for from five to eight hours in a room of from 30 to 40 cubic m.

In *experimental malaria*, Celli found that euquinine and methylene blue had the best prophylactic effect. It may therefore be suggested that practical experiments be made with these drugs.

According to Fontana and Di Mattei, lemon juice (a decoction of lemon peel with the addition of 10 or 15 per cent. of glycerine) had a good prophylactic effect, attributable to the fact that if continually taken it imparts a peculiar smell to the skin and secretions which is repulsive to mosquitoes. It should be taken every morning in water fasting, the dose being a teaspoonful for an adult and half a teaspoonful for a child.

D'Abadie reports that according to an Ethiopian popular belief, the correctness of which has been confirmed by many other observers, the daily exposure of the naked body to fumigations of sulphur affords a protective measure against malaria.

The *thorough treatment and cure of* all malarial patients is also important to successful prophylaxis, for every sufferer from malaria forms a danger to those around him.

TREATMENT.

It should be an axiom, especially in warm countries, to treat even the mildest cases of malaria carefully and not *en bagatelle*, as is often done, because even from the mildest illnesses the severest forms may develop.

Quinine is the principal remedy for malaria, and is used in all its forms. The effect of quinine is that it attacks the malaria parasites direct, checks their development and destroys them. Binz, in 1867, proved that quinine exercised this effect on subordinate organisms, infusoria and fungi, which are known to be the cause of the processes of fermentation and putrefaction. According to Golgi, Ziemann, &c., the young, extra-globular parasites are most susceptible to the action of quinine. On the other hand, the crescents are quite uninfluenced by the drug.

Schellong does not regard quinine as a specific in malaria. According to his opinion it operates on the red blood corpuscles by attracting away the oxygen, thus indirectly destroying the malaria parasites by withholding the oxygen from them.

The *dose, manner* and *time of administering quinine*, are of great importance.

As regards the *dose*, the administration of small occasional doses has now been quite relinquished in favour of single larger doses at longer intervals. In mild forms 1·0 gram. is the usual dose for adults ; in serious forms 1·0 to 2·0 are administered. Experience has taught us that it is useless, and even may prove dangerous, to exceed this quantity. The enormous doses (8·0 grams. or even 10·0 per diem were formerly given) have now been generally given up. In children 0·1 gram. is ordered for every year of life ; in children under 1 year old 0·1 is the dose.

It sometimes happens that after large doses of quinine given to young excitable people—sometimes even after smaller doses—toxic symptoms set in, which, however, as a rule, again disappear after discontinuing the drug. The symptoms most frequently consist of singing in the ears, hardness of hearing and even complete deafness (caused by congestions and hæmorrhages into the labyrinth). More rarely there is palpitation in the head, giddiness, fainting, anguish, restlessness, tremor of the hands, amaurosis, a bitter taste in the mouth, palpitation of the heart with flushing, increased, weak and irregular action of the heart, dilation of the pupils, a cold skin and cutaneous eruptions, more especially urticaria. Quinine amaurosis is apt to develop suddenly, and is apt to be more or less complete. According to Yarr, the pupils are dilated and insensitive to light. The fundus oculi, in serious cases, appears pale, the optic disc livid, and the retinal vessels as thin as a thread. The blindness may continue for a few hours or persist for several weeks. The power of vision returns slowly, but restriction of the field of vision, and reduction of the perception of light and the sense of colour mostly are left, and atrophy of the optic nerve may result. In Cuba, where heroic doses of quinine

are the order of the day, this, according to Fernandez, is not rarely observed. When amaurosis occurs, quinine, of course, should be immediately discontinued, and nitro-glycerine should be substituted.

In order to avoid singing in the ears and hardness of hearing, Fisch recommends bromal hydrate (10 to 20 drops in sweetened water immediately after taking quinine) as it also contributes to the solution of the quinine.

Under certain circumstances (F. Plehn) fever is caused and maintained by the continuous use of quinine (*quinine fever*). This is probably the case with many patients in whom fever persists, notwithstanding the administration of large doses of quinine. In such cases it is not a question of arousing latent malaria parasites circulating in the blood according to Steudel, who regards quinine in larger doses as an excitant of malaria in latent infection, for quinine fever also occurs in persons who are not suffering and have never suffered from malaria. F. Plehn is of opinion that quinine sets up a disintegration of the blood corpuscles, especially in persons whose blood cells are abnormal, more especially from malaria ; in the mildest cases this is hardly perceptible, but in serious cases it may cause hæmoglobinuria. In quinine fevers no parasites are found in the blood and signs of quinine intoxication are present.

Of the various quinine preparations hydrochloride of quinine and the bisulphate of quinine are the most suitable on account of their solubility. These may be introduced into the body in different ways. The usual manners of administration are :—

(1) The *internal method.*—Quinine is best administered in wafers or Japanese paper, and a few drops of hydrochloric acid should be taken afterwards. It may also be taken in the form of pills (freshly prepared) or it may be taken in solution. Milk and sweetened black coffee are suitable vehicles for concealing the bitter taste of quinine. Quinine pearls (small, flat gelatine capsules) and quinine-chocolate-pastiles, as also the tasteless Euquinine are from the quinine manufactory of Zimmer and Co., of Frankfort a. M., are recommended for children. Compressed tablets are not recommended, as they are sometimes passed undigested with the stool. The daily dose is given according to occasion once or twice within an hour.

Tannate of quinine only contains 30 to 32 per cent. of quinine, and must be given in doses three times as large as the other salts. This preparation is occasionally preferred on account of being almost tasteless. Taking its insolubility into considera-tion, it is, however, doubtful if it possesses great value. Kohlbrugge approves of it because he could administer large doses (he gave up to 8·0 grains per diem) without causing symptoms of intoxication ; this perhaps is to be attributed to its insolubility.

Should the patients suffer from vomiting it is advisable to add a little opium or morphia to the quinine. It is well to give the dose just after an attack of vomiting and to prohibit the patient taking food for the next half hour. The vomiting, however, is often so obstinate that the patients cannot keep it down, and in that case, as well as for other reasons, viz. : inability to swallow from coma, eclampsia, &c., when administration by the mouth is impossible, other means must be resorted to. These are :—

(2) *Administration per rectum.*—The enema should consist of 100·0 grams. mucilage, to which 10 drops of tinct. opii are added. This should be given twice, at intervals of half an hour. For children in particular. suppositories are also advised, the dose being the same as by mouth.

(3) *Subcutaneous injection.*—This method is employed principally when the symptoms are alarming, and for this purpose quinine bihydro-chloride (carbamide) and quinine hydrochloro-sulphas are most appli-cable by reason of their solubility without acid ; they are both soluble in equal parts of water and are mostly injected in a proportion of 1·2 to 4.

Hertz, for subcutaneous injections, recommends amorphous hydrochloride of quinine, a brown, easily soluble powder, 1 in 4. Köbner advises hydrochloride of quinine 2·0, glycerine, distilled water āā 4·0 (without acid), to be warmed before use, as the

mixture congeals when cold.   Laveran and other French doctors order quinine
hydrochlor. 3·0, antipyrin 2·0, aq. dest. 6·0.

In this method of application half of the internal dose is sufficient.

The subcutaneous injections have the disadvantage of being painful,
and, even if made with strict antiseptic precautions, are apt often to cause
local inflammations, infiltrations, abscesses, and even cutaneous gangrene
(Schellong, F. Plehn, Ziemann). The subcutaneous method of application
has therefore been much relinquished lately, and in its place :

(4) *Intra-muscular* (glutei muscles) *injections* with the same salts are
preferred owing to the fact that they cause less local irritation than the
subcutaneous method.

According to Xibitia the local inflammations are really useful.   This author
observed that, in rebellious forms of malaria, recovery ensued when *abscesses* had
been caused by subcutaneous injections, and he is of opinion that phagocytosis is
encouraged by the increase of white blood corpuscles during the development of the
abscesses.

(5) *Cutaneous applications* are recommended by Rasch in the form of
inunctions of alcoholic solutions of quinine, by Feuchtwanger in the form
of *inunctions of ointment* (1 in 20) especially on the back, the inside of the
thigh, in the axillary or inguinal regions ; this method is particularly
applicable to children.

(6) *Intravenous injections* (Baccelli).—For this injection a vein at the
bend of the elbow is chosen. First of all a constricting bandage is
applied above the elbow, the needle of the syringe is then inserted into
the vein, the bandage is loosened before the liquid is injected, which is
then done very slowly, and the small wound closed with collodion.
Naturally antiseptic precautions must be used. The solution which,
according to Baccelli should be used tepid, consists of hydrochloride of
quinine 1·0, chloride of soda 0·075, distilled water 10·0, the solution must
be boiled and filtered before use. The symptoms of intoxication which
may set in immediately afterwards usually vanish after a short time.

Of these different methods of application, the *internal* administration is
the most important and the method most frequently employed. If, for the
reasons given above, this cannot be made use of, *intramuscular injections*
occupy the second place. The remaining methods are but seldom made
use of.

The *time for using quinine* depends on the type of malaria from
which the patient suffers.

In the ordinary intermittent fevers, it is regarded as a rule not to
administer quinine during the attacks, but *during apyrexia*. It has
been practically proved that quinine is most effective when given four to
six hours before the time when the next attack is expected, so that the
complete absorption of the drug is coincident with the development of
the youngest brood, which is most susceptible to the action of quinine.
As a rule, not the first attack, but the subsequent attacks are thus
checked. With subcutaneous, intramuscular and intravenous injections,
in which the action of the quinine is more rapid, it is given one or two
hours before the expected attack. In order to prevent relapses or latent
malaria the use of quinine must be continued several days after even the
mildest attack is checked, and for this purpose 1·0 gram. in the morning
or 0·5 night and morning will be found most suitable.

In *malignant tertian fever, tropical malaria*, Koch advises that quinine
be given after the attack of fever, namely, in that stage of development
of the parasites preceding sporulation, when the adult ringed parasites
appear in the blood. If given at this time, 1·0, according to Koch's
experience, suffices to clear the blood of the parasites. One more attack

as a rule supervenes, but it is milder and more irregular than the previous attack, and no more parasites are, as a rule, found in the blood. Koch designates these attacks "after-fevers," and believes that they originate from the elements of the dying parasites and the poisonous products of metabolism present in the same. Anyhow, he is of opinion that the attacks are originated not by the young generation but by the old generation in the process of perishing. At the conclusion of the "after-fever" one more dose of 1·0 is given, and to prevent relapses 1·0 should be given, continued every fifth day for a month or six weeks.

In *remittent* and *continued fevers* the effect of quinine is less apparent and more uncertain than in the intermittent form, but nevertheless, it is the most efficacious medicament known. In remittent fevers the periods of remission are chosen for the administration of the quinine. In continued fevers the period of pyrexia must not be waited for, but under all circumstances in which a high temperature has persisted for two days, 1·5—2·0 of quinine must be given, and the dose repeated on the following days ; or 0·5 may be given every six hours, or 1·0 every twelve hours. Relapses should be sought to be avoided in the same manner as in malignant tertian fever.

If the fever, after three or four days, shows no tendency to abate, F. Plehn advises a careful examination of the blood to determine if "quinine fever" be not present (see p. 163). If no parasites are found after several examinations, quinine is discontinued and the activity of the skin and kidneys excited by hot baths and copious quantities of aerated fluids.

In the *pernicious forms* of fever, not including blackwater fever, in order not to waste precious time, quinine must be given immediately, and should be used in the same manner as in continued fevers.

In regard to the *treatment of blackwater fever*, there are two opinions directly opposed one to the other. According to the one opinion, which was especially adopted by the older French colonial doctors, and which has lately found a great champion in Steudel, blackwater fever, like every other malarial disease, should be treated with quinine, and as it is a serious form of fever the doses should be large. Steudel gave his patients up to 8·0 grams. per diem. The second opinion, on the other hand, which has now been adopted by the more modern French colonial doctors, and principally by a number of German doctors (Kohlstock, F. Plehn, A. Plehn, &c.) and now counts most followers, is supported by the above-mentioned relations between blackwater fever and quinine, and therefore entirely discards the use of quinine in this disease. According to the observations of the investigators mentioned, blackwater fever treated without quinine exhibits a shorter course, less important sequelæ and a lessened mortality than when treated with quinine. In Cameroon, Kohlstock, when treating blackwater fever without quinine, had no death out of 8 cases. F. Plehn had one death out of 25 cases, = 4 per cent. A. Plehn had five deaths out of a total of 53 cases, = 9·8 per cent.

During the same period 35 cases were treated outside the hospital by other methods, therefore, doubtless, almost or mainly with quinine ; of these 15, = 43 per cent. died. Döring had five deaths amongst 40 cases, = 12·5 per cent. F. Plehn treated 12 cases without quinine on the Tanga Coast (German East Africa) and did not lose one. A comparison of these figures certainly decides in favour of treatment without quinine, which, besides, is unnecessary, for blackwater fever possesses a pronounced tendency for spontaneous recovery, seeing that the malaria parasites perish during the disintegration of the blood corpuscles ; F. Plehn was the first to direct attention to this circumstance. It is only permissible

to give quinine after the disappearance of the fever and the nephritic symptoms, and when the patients have been feeling well for several days, when it is used in the manner already mentioned (p. 164) to prevent relapses. Should albuminuria persist quinine should be entirely discarded on account of the irritation it exercises on the kidneys. In the severe forms of fever of the tropics it is advisable to assist the effect of quinine by administering *aperients*, more especially *calomel* (0·3 to 0·6) before or with it. Buchanan (India), who has had vast experience, says : " Without the preliminary purge I have seldom seen quinine do any good."

Quinine has recently been much used in the form of *euquinine*, the ethyl-carbonised acid of quinine, being preferred on account of its tastelessness. It is a white crystalline, very voluminous powder, that is difficult to dissolve in water. It has a less irritating effect on the digestive organs, but its actions otherwise are the same as quinine, namely the toxic effect on the red blood corpuscles (A. Plehn). The same dose is used as in quinine (F. Plehn). Gray [1] is even of opinion that in efficacy it exceeds quinine. Euquinine is administered in wafers, cocoa, chocolate, tea or water.

Of the other numerous alkaloids of cinchona bark, sulphate of cinchonidin has proved of most service, it has to be given in doses of one-third to one-half larger than quinine.

The following *substitutes for quinine* are used :—

Methylene blue (medicinal) was first recommended by Ehrlich and Guttmann, who gave daily 0·5 to 0·7 in gelatine capsules up to 1·0. Methylene blue (which, according to the investigations of Valvassori, Peroni, Parenski and Blatteis, especially attacks the parasites of irregular fevers and the crescent bodies) is, like quinine, administered in the intervals of fever, and its use is continued for eight to ten days after the cessation of the fever. Parenski and Blatteis also recommend it subcutaneously, giving daily two injections of a 5 per cent. solution = twice 0·05. F. Plehn found it very uncertain in its action. Koch recommends its use in blackwater fever (1·0 per diem). Beck advises a combination of quinine with methylene blue. The transient irritation of the bladder originated by methylene blue is combated by a little nutmeg on the point of a knife administered daily. The urine, after taking methylene blue, assumes a green or blue tint, which disappears on the addition of alkali, and this phenomenon persists for two to eight days after the discontinuance of the remedy. The freshly evacuated stool exhibits the ordinary colour, but after a few moments the surface bcomes bluish-green. Headache, loss of appetite, vomiting and diarrhoea, are further symptoms that methylene blue may cause. According to Ollwig, new methylene blue (hydrochlorate diäthyltoluthionin) causes no secondary symptoms if administered in a rational manner, that is to say in the afebrile period, and if the entire daily dose (0·5 to 1·0) be given within a few hours.

Hydrochlorate of phenol is recommended, especially by Italian doctors ; 1·0 to 4·0 being given daily in doses of 0·5. A. Plehn. F. Plehn, and Ziemann found this drug ineffective. Besides, it may occasion disburbance of vision, exanthema, palpitation of the heart, cyanosis, hæmoglobinuria (F. Plehn) and even collapse.

Creosote, in the form of inunctions, is recommended by Fitzgerald ; in children 15 to 20 drops, mixed with an equal proportion of olive oil, are rubbed in once daily. For adults 30 to 60 drops, to which an equal amount of olive oil is added, are rubbed in every day. In children particularly the effect of creosote is said to be both rapid and favourable, and relapses are believed to occur much more rarely than with other methods of treatment.

Eucalyptus globulus is mostly used in the form of tincture.

Helianthus annuus (leaves and flowers) as an alcoholic tincture or alcoholic extract, was found by Moncorvo to be very effective in the case of children.

Pambotano-root (Calliandria Houstoni, Bentham), which is used in the form of watery and alcoholic extract, is said by Dinan to be superior in most cases to cinchona bark and its alkaloids.

Ficus ribes—Reinward (bark), in the form of a decoction, is a Malayan remedy for fever which, according to Kohlbrugge, is of value.

Neem oil (azadirichta indica).—Spencer used this in chronic malaria, after discarding quinine and arsenic, and found it very effective. Five to ten drops are given three times daily in milk or peppermint water. Spencer also recommends the juice of the leaf of the *Mexican poppy (argemone mexicana).*

We shall have to wait to see if in the future any of these drugs will play a larger

[1] *Brit. Med. Journ.*, 1898, February 26.

part. I may, however, remark that they are far behind quinine in efficacy, and the same applies to "*quinium*," which is advocated in France, and consists of an extract of cinchona rind prepared with alcohol and lime. This preparation is recommended in chronic, obstinate and relapsing cases, and in cachexia. It is made up into pills or boluses of the strength of 0·15 to 0·5, of which from 2 to 10 are given daily. *Warburg's tincture* is largely used by English doctors ; according to Roux it is a combination of quinine, angelica, cubebs, camphor, sassafras, rhubarb, myrrh and saffron ; this mixture cannot compare with quinine as regards effectiveness.

Next to quinine the most important remedy for malaria is *arsenic*. As already mentioned, this drug, unlike quinine, does not influence the malaria parasite directly, but is given on account of its tonic effect. It is indicated in old, obstinate, and frequently relapsing intermittent fevers, in cachexia and in neuralgia, which do not yield to quinine. The favourite preparation is Fowler's solution, of which from 2 to 10 drops are administered three times a day ; the dose being increased daily by one drop. Arsenic has the best effect when given in conjunction with quinine.

Baccelli's mixture is a combination of quinine and arsenic compounded as follows : sulphate of quinine 4·0, potassium ferri tartarata 10·0, arsenious acid 0·1, water 300·0. On the first day after defervescence, a tablespoonful is given every hour, on the second day every two hours, on the third day every three hours, and so on, until finally it is only given night and morning.

According to Hertz arsenic is contra-indicated when digestive disorders are present in pernicious fevers and in old people.

In obstinate cases of malaria with large splenic tumour, in which quinine and arsenic has proved inefficient, Jacobi [1] orders *ergotin* (with or without quinine).

The *symptomatic* treatment of malarial disorders is not so important as the *specific* treatment, but it is also not without importance. The nursing is of great consequence. Sometimes malaria is cured in hospital under the influence of better nourishment and rest in bed even without quinine (Nocht).

In *simple intermittent* fever no special treatment is necessary. The patients must keep their bed during the attacks ; during the apyrexia they may get up, but not unless there is absolute apyrexia. They should be given invalid diet, consisting of digestible strengthening foods, mostly in liquid form.

In *severe rigors* the bed should be warmed, the patients should have a moderate quantity of warm drinks given them, and their skin should be rubbed with hot flannels. Should the rigor persist, F. Plehn recommends a hot water bath or a Quincke's hot-air bath.

In severe cases the *hot stage* may necessitate a cool bath (23—27°).

In the *sweating stage* perspiration should be encouraged by wrapping the patients in blankets and giving them a large quantity of hot drinks.

An emetic of ipecacuanha is sometimes given to relieve the *stomachic disorders* setting in at the commencement of the attack.

Severe *vomiting* should be combated by effervescing mixtures, fragments of ice, opium, morphia, tincture of iodine (2 drops in water), or by counter-irritation over the region of the stomach, such as mustard poultices, mustard leaves, &c. Gray recommends, when the vomit is bilious and has an alkaline reaction, diluted hydrochloric acid in 10 to 15 drop doses every half hour or every hour.

In *constipation* a mild aperient, such as castor oil, calomel (0·3—0·6), seidlitz powder, &c., should be given.

When *diarrhœa* is present, calomel is recommended.

Intestinal hæmorrhages necessitate rest, ice, and opium and ergotin, subcutaneously if necessary.

[1] *Med. News*, 1898, October 22.

In *headaches, lassitude, and pains in the limbs* antipyrin (0·5) gives good results, and if necessary, may be repeatedly given. Beck recommends methylene blue (0·3) for headaches.

Restlessness and *sleeplessness* are combated by bromide of potassium (2·0 to 5·0 within an hour), or by chloral hydrate (1·0—1·5) ; cold packs also have at times beneficial effects.

Röwer recommends sufferers from malaria, when exposed to injurious influences, which experience teaches us may cause relapses, to take a hot bath. "By the dilatation of the cutaneous vessels the internal organs are considerably relieved, particularly those that play so large a part in malaria, namely, the liver and spleen ; while cold baths drive the blood to the internal organs, and are apt to cause relapses of fever." Every person who has experienced the benefits of the hot bath is able to agree with Röwer's advice.

In *remittent and continued fevers* cold baths and antifebrile drugs, such as antipyrin (1·0—2·0), antifebrine (0·3—0·5), phenacetin, &c., are indicated when quinine fails to reduce the temperature. In regard to antipyrin, which is freely used in the tropics on account of the rapid amelioration it affords, it must be particularly noted that it is only a symptomatic remedy, and does not affect the disease itself.

Atkinson, in very high fever, with unconsciousness, recommends ice-packs. The patients are laid on a mackintosh, covered with a sheet dipped in ice-water, the entire body is packed in ice, and an ice bag applied at the same time to the head.

In the therapeutics of the *pernicious forms*, besides quinine strong stimulants, such as champagne, cognac, strong wine, black coffee, ether and camphor, play a large part.

In the *algide form* hot baths and packs are indicated in addition, and in excessive diaphoresis, atropine (0·005—0·001 subcutaneously), or of agaricin, may be tried.

In the *cerebral forms*, ice-bags are applied to the head, and cold baths and douches to the body. In addition to these relief by means of stimulating enemata, counter-irritation to the extremities, narcotics (opium, morphia, chloral hydrate, bromides), may be tried, and local bleeding (15 to 20 leeches over the mastoid processes) when the face is flushed. Simultaneously one must endeavour to give the patients a plentiful supply of liquids.

The *cardialgic form* requires subcutaneous injections of morphia.

In the *choleraic form* injections of warm solutions of tannic acid (15·0 to 20·0 in from ½ to 2 litres of water) are to be tried, as well as hot baths or packs.

Malaria dysenterica is sometimes favourably influenced at the beginning of the illness by calomel. Subnitrate of bismuth and naphthalin are also occasionally efficacious. Later on opiates must be given. A milk diet is necessary.

In *pneumonic and pleuritic malaria* expectorants with narcotics are necessary.

In *blackwater fever* one must endeavour to excite diuresis by a plentiful supply of liquids (especially mineral waters and milk) ; large enemata serve the same purpose. Restlessness and insomnia are treated by chloral hydrate, the vomiting with fragments of ice, opiates, morphia and tincture of iodine. Mense recommends the use of a tube from which the patients can drink. On the slightest sign of heart failure, digitalis, strophanthus, caffeine, camphor with benzol, &c., are indicated. In distressing dyspnœa, F. Plehn recommends inhalations of oxygen as advised by Kohlstock. When uræmic symptoms supervene wet packs are applied.

If anuria sets in, F. Plehn advises that the intestinal action should be stimulated by calomel and saline aperients. Döring, indeed, in all severe cases, advocates Carlsbad salts (one tablespoonful to a wineglassful of water). French doctors (Quennec and others) have lately prescribed chloroform (4·0—6·0 in 250·0 of mucilage mixture, a sip every ten minutes till improvement sets in). The value of this remedy is supposed to rest on its ability to dilate the vessels and thus relieve the congested portal venous system. According to the latest reports, however, chloroform has not fulfilled expectations. Steudel, as a last resource, advises transfusion of blood, and believes that he saved the life of one patient by this means. Iron and arsenic are administered for the anæmia that is left. In nephritis, rest in bed and a milk diet are indicated.

Of the *masked forms* of malaria only a few require symptomatic as well as specific treatment.

In *inflammation of the lymphatic glands*, according to Martin, quinine, arsenic and iron, are recommended. Priessnitz's applications with incision and enucleation are undertaken when suppuration occurs. Inflammation of the testicle and epididymis is treated by elevation of the part, ice, or other local applications.

In *post-malarial weakness*, besides quinine (0·5 every five days), arsenic and iron are administered. Iron is given, according to circumstances, in the form of Blaud's pills or liquor ferri albuminatus (Drees). The arsenical iron waters of Levico and Roncegno also may be taken with advantage.

Cold douches are mostly recommended for the splenic tumours. Hertz combines baths of from fifteen to twenty minutes' duration at a temperature of 27° to 30°, or with cold jet baths—the latter lasting one minute or one and a half minutes. Priessnitz's applications (at night), the induction current (daily for five to six minutes), massage, subcutaneous injections of iodine with iodide of potassium may be tried. Parona recommends iodine 0·25, iodide of potassium, guaiacol, āā 2·5, sterilised glycerine 25·0, daily, 1·0. Intramuscular injections of carbolic acid, arsenic, ergotin, strychnine, and especially quinine, every two or three days, are brought into requisition.

The *extirpation of the spleen* has been recommended. Of six patients operated on by Majerowitsch and Nannoti, four recovered. Generally the lymphatic glands take upon themselves the functions of the extirpated spleen and enlarge. The bone marrow is presumed to also assume a similar functional *rôle* (Laccetti).

Bragagnolo regards advanced malarial cachexia, leucæmia, severe hepatic and renal affections, and extensive adhesions, as contraindications to removal of the spleen.

Hepatic affections require treatment by natural or artificial Carlsbad waters.

Change of climate is one of the most important and, in many cases, even the only means of treatment for malarial diseases of warm countries. In the obstinate milder forms (intermittent, masked, initial cachexia) a change of residence, if only a few miles distant, may suffice, without regard to the salubrity of the selected place, to cause the illness to disappear. Of still more favourable influence is a change to a hill station, or to a spot known to be healthy. It is therefore urgently necessary that sanatoria should be erected on healthy places, where convalescents from malaria and other complaints may be taken in and cared for. It is advisable to build such sanatoria at a height of from 500 to 1,000 m. A steep, dry and malaria-free locality should be chosen. Too high a locality is not advisable, as experience has taught that the hill stations of India, situated at an altitude of from 2,000 to 3,000 m., are not suited to patients with heart and lung diseases, or who are suffering from rheumatism and dysentery.

Koch's experience contradicts the generally received opinion as to the utility of sanatoria. According to his views it is all the same if a person with parasites in his blood is on the plain, on the coast, or on the mountains. As long as his blood contains parasites he will again get fever, independent of the district where he is staying. This is certainly correct, but it is by no means all the same if the parasites present are being continually added to, or if the patient is protected from fresh invasions of parasites by being transported to a sanatorium in a malaria-free district.

The increase of the *hæmoglobin constituents* of the blood observed in European mountainous districts has not been confirmed in similar districts within the tropics. This was not confirmed either by Kohlbrugge[1] in Tosari, East Java (1,777 m.) nor by A. Plehn in Buca in the Cameroon Mountains (1,000 m.). Plehn even found a decrease of hæmoglobin in anæmics at that altitude.

Journeys to a more northern subtropical region (Japan is the much favoured place of the tropics of Asia) is of just as much service as residence in a sanatorium; *voyages in the Southern waters* are also of great benefit. But the *return to Europe* has the most beneficial effect, and is indicated in every case of advanced malarial cachexia, in intestinal diseases, in diseases of the lungs and lymphatic glands (Martin), and after recovery from pernicious forms of disease, more especially black-water fever. If nephritis remains after hæmoglobinuria, or if there is a pronounced idiosyncrasy to quinine, it is necessary to send the patients home (F. Plehn). In other cases the patients must stay at least a month in a mountain sanatorium or must take a sea voyage. Naturally, during the acute stage, the patients cannot travel, but if possible they should be removed from the fever-zone, as, for instance, from the coast, to the open sea. Däubler[2] recommends the erection of sea hospitals as well as of mountain hospitals, the former to be on ships anchored out as far as possible; these have been used by the Dutch with good results.

According to F. Plehn, regular albuminuria with the attacks of fever (probably the consequence of renal lesions) is a further indication for change of climate.

Summer is the most advantageous time for the return to Europe and should be spent by the patients in the mountains: the Hartz Mountains, the Black Forest, Riesengebirge, Fichtelberg, the Lake of Lucerne, &c., are the best places of resort for the patients, and the use of chalybeate baths such as Liebenstein, Steben, Alexanderbad, Schwalbach, &c., may be suitably combined with the stay. A course of treatment in Carlsbad, Marienbad, Neuenahr, Kissingen, Wiesbaden or Schulz-Tarasp, are recommended for hepatic and splenic disorders. Fayrer, who has had vast experience, advises everybody who has lived many years in India to go to Carlsbad for the " cure," whether he intends returning to the tropics or staying at home. A few weeks, however, must be allowed to elapse for establishing re-acclimatisation in the temperate climate before taking the " cure " (see p. 121). If relapses of fever set in a change of place is advisable.

Some patients stop in the south of Italy, or on the Canary Islands during the first winter, as a colder winter climate cannot be borne by persons who have passed many years in the tropics. This is especially the case in regard to old people, for whom change of climate is a serious matter. Deaths from severe malarial relapses or pneumonia are not at all rare immediately after old tropical residents reach home.

[1]   *Corresp. Bl. für Schweizer Aertzte*, 1897, No. 15.
[2]   *Die Grundzüge der Tropenhygiene*, p. 65.

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In Hirsch, i., p. 211, there is a compilation of the very extensive literature.

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VIII.

BERI-BERI.

DEFINITION.

By the term *beri-beri* is understood a disease which appears endemically and epidemically, especially in the tropical and subtropical regions of Asia, Africa, America and Australia. Its principal symptoms consist of disturbance of motion and sensation, dropsy, and an affection of the heart. The symptoms are attributable to degenerative changes of an inflammatory nature in many of the peripheral nerves. The main features of the disease consist of perversity of motor and sensory functions.

NAMES.

The word *beri-beri* is variously explained. According to the best known and oldest definition, it is derived from the Hindostani word *beri*, signifying sheep, and is applied on account of the uncertain staggering gait of beri-beri patients, which has a resemblance to the unsteady movement observed in the walk of the sheep. The English sometimes term it *barberi, barbers ;* the French, *barbiers.*

The following are other names for the disease: *Loempoe* in Java, *Pantjakit niloe* or *siloe, i.e.,* crystal disease ; *Binas Apooi* in Banka ; *Pantjakit papoea* on the coast of New Guinea ; *Kaki lem but, i.e.,* weak legs, in Malay ; *Kakke, i.e.,* disease of the legs, in Japan and China ; *Ashite* (same meaning) in Japan ; *Maladie des sucreries* in the French Antilles ; *Hinchazon de les negros and chinos, i.e.,* dropsy of the negroes and Chinese, in Cuba ; *Perneiras, i.e.,* foot disorder, and *Inchacao, i.e.,* œdema, in Brazil ; moreover, *Hydrops asthmaticus* (Rogers), *Lynclonus Beri-beria* (Mason Good), *Myelopathia tropica scorbutica* (van Overbeek de Meijer), *Paraplegia mephitica* (Swaving), *Sero-phthisis perniciosa endemica* (Wernich), *Neuritis multiplex endemica* (Scheube), *Panneuritis endemica* (Bälz).

HISTORY.

The history of beri-beri can be traced back to ancient times, and indeed the first news of the disease came from China. In a Chinese pamphlet of the second century, kakke was already mentioned, and another of the seventh century contains a minute description of the disease. It was perhaps also known to the Romans ; two passages of Strabo and Dio Cassius relating to the campaign of the Roman army under Aelius Gallus in Arabia, 24 B.C., when describing the illnesses which attacked the soldiers on the Red Sea littoral, refer to an ailment closely resembling beri-beri.

GEOGRAPHICAL DISTRIBUTION.

(See Map II.)

A study of the geographical distribution of beri-beri shows that the disease extends over a large part of the tropical and subtropical countries in the eastern as well as in the western hemisphere; beri-beri has also been met with in the temperate zone.

In Asia the Malayan Archipelago forms one of the principal centres of beri-beri. In these islands the disease is endemic, but it periodically appears epidemically, as in Sumatra, where, in Atjeh, the Dutch troops suffer severely from it. Beri-beri is also endemic in the plantations of the East Coast of Sumatra and in the Lampong districts; in the islands of Bintang, of Banca (particularly in the mining districts), and of Billiton; in Borneo beri-beri prevails on the coast at Sambas, Sampit and Bandjermassing, and in the interior at the mining districts of Sintang and on the island of Labuan. In Java, where beri-beri has prevailed to any marked extent for only a few decades, the disease is particularly severe at Batavia and on the island of Onrust, and in the district of Banjuwangi; in the Celebes, especially in the district of Macassar; in the Moluccas, more particularly in Amboina, Saparna, Banda, on the south coast of Ceram and in New Guinea.

Beri-beri is likewise endemic on the Solo Isles, situated between Borneo and the Philippines, and also in Mindanao. In Manila beri-beri was unknown until 1882 or 1883, when a severe epidemic occurred and where it now prevails endemically (Maseras).

In India the principal seat of the disease is in the northern provinces, especially on that strip of land between Masulipatam and Ganjam, where it occurs endemically, more especially on the coast and in the plain between it and the mountains. Beri-beri exists, but is far more rare, on the Coromandel Coast, in the lowlands of the Carnatic and on the Malabar Coast. It has also been observed in Calcutta and in various parts of the Province of Dakka and in Assam, in the central provinces.

In Ceylon beri-beri formerly raged with such severity that it was styled "the bad sickness of Ceylon." It has been less prevalent in Ceylon of late years.

As to Further India, the disease is frequent in Burmah and Siam; it also occurs in Penang, Singapore, on the islands situated off the coast of Cochin-china, particularly Pulo-Condor, and in Saigon, Choquan and Hué (Annam).

In China, according to Manson, beri-beri has been observed in Shanghai, Soochow, Wenchow, Foochow, Formosa, Amoy, Swatow, Fatshan, and Hongkong, where in 1888-1889 an extensive epidemic raged. According to Lynch,[1] cases of beri-beri also occur every summer in Chinkiang.

In Corea the disease occurs principally in the south.

Japan is one of the chief centres of beri-beri. The disease has an extensive endemic area on the main island, Hondo, where the large cities and the towns situated near the sea coast form its principal seat. During the last few decades there has been, however, a remarkable spread of the disease, which is now met with even endemically in the central provinces, Kodzuke and Oshiu, and in the mountainous province of

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[1] China, *Med. Rep.*, 1894.

Shinano. In the northern island of Yezo, which, on the whole, enjoys a temperate climate, and has a winter of six to seven months' duration, beri-beri is frequently met with, whereas it appears more rarely on the southern island of Kiushiu. The disease also exists in epidemic form amongst the fishermen on the Kurile Islands, where the climate is so cold that the grain does not ripen (Grimm).

From the *African* Continent, where beri-beri most probably is distributed to a much greater extent than has hitherto been supposed, reports as to the occurrence of the disease have only lately been furnished from the following places: Senegal (Lasnet), Gorée (Firket), Sierra Leone (F. Plehn), Togo (Döring), Niger (Castellote), Soudan (Suard), Cameroon (Zahl, F. Plehn, Lichtenberg), Gaboon (Calmette, Duchâteau), Loango (Firket), Congo (Sims, Mense, Dryepondt), Angola (Dapper), in West Africa from the Tanga Coast (F. Plehn), and in East Africa from Zanzibar (Manson), and even in Natal at Pietermaritzburg. The disease has been met with on several adjacent islands ; Madagascar, Nossi-Bé, Réunion, and Mauritius.

In Australia the disease has lately been observed in several places, mostly amongst the Chinese (in Sydney, Melbourne, Wyndham, Kimberley), also in New Zealand ; quite lately there are reports as to its occurrence in New Caledonia (Grall, Porée, and Vincent), on the Fiji Islands (Bolton), and on the Sandwich Islands (Vineberg).

In America, Brazil forms the principal seat of beri-beri, where during recent decades it has spread, not only along the entire coast line, but it has also penetrated into the interior, more particularly in the provinces of Pará, Minas-Geraes and Matto-Grosso. The disease has also been observed in Paraguay, Cayenne,[1] Venezuela, amongst the labourers on the Isthmus of Panama, on the Antilles, particularly on Guadeloupe and Cuba. Finally it must be mentioned that, according to Hirsch, a few cases have also been observed in San Francisco, California.

Lately beri-beri has also been observed *in Europe*. I cannot concede, however, that the epidemic of scurvy described by Dechambre as occurring during the siege of Paris amongst the military garrison, and which in a few cases exhibited beri-beri-like symptoms, was actually beri-beri. On the other hand, the epidemic which occurred in the overcrowded Richmond District Asylum in Dublin in 1894-1898, as described by Norman, was undoubtedly beri-beri, notwithstanding the fact that its origin has not been elucidated.

Cases of beri-beri are no rareties in the larger English and German harbours on ships arriving from the tropics. As Dublin is a port that has commercial connections with the entire globe, it is quite possible that the disease may have been thus imported, though it escaped observation. Such a coincidence is not surprising when one takes into consideration that some time may have elapsed between the period of the introduction of the disease and the outbreak of the epidemic, which was unobserved at its commencement. It is to be noted also that it is often difficult or quite impossible to extract from mental patients the history of their disease.

The first outbreak in Dublin occurred in 1894. No minute information of its commencement can be given, as many mild cases were doubtless overlooked. Altogether there were 174 cases (out of a total of 1,503 mental patients) ; of these 127 were men and 47 women. The cases of disease increased from June to September, and decreased rapidly in October, completely ceasing in November. Amongst the cases many were severe, with acute cardiac insufficiency, general dropsy, and marked symptoms of paralysis ; 18 men and 7 women died, giving an average mortality of 14·3 per cent.

[1] According to a recent publication of Fowler, the disease also appears to be endemic in British Guiana.

In 1895 no fresh cases came under observation, but in July, 1896, during which year the mean number of inmates was 1,686, the disease broke out anew, increasing up to September and continuing into the following year. A total of 114 persons were attacked, namely, 31 men, 83 women (amongst them 7 female attendants); 2 men and 6 women died (no female attendants) = 7 per cent. The epidemic was milder than that of 1894 ; acute cardiac insufficiency and general dropsy were rare, and the motor disturbances less pronounced.

In 1897, the mean number of inmates being 1,800, the disease assumed larger dimensions. A total of 246 persons fell ill, 47 men and 199 women, amongst them being 2 male attendants and 6 female attendants, the distribution in months being as follows : 4 cases in January (though these might be reckoned as appertaining to the epidemic of the previous year), 134 in July, 50 in August, 7 in September, 3 in October, 37 in November, and 6 in December. The cases were mostly of the milder form of the disease ; the mortality only averaged 4·4 per cent., 3 men and 8 women succumbing ; none of the sick attendants died.

In 1898, with the exception of a number of cases of relapse, only 13 fresh cases of the milder form amongst the female inmates came under observation.

Almost simultaneously with those in Richmond Asylum, Dublin, beri-beri-like diseases were observed in several other lunatic asylums of England and America. The disease was observed in the Suffolk County Asylum at Melton (Suffolk) in the winter of 1894-1895, and 1896-1897 ; in the lunatic asylum of Sainte-Gemmes-sur-Loire in the summer of 1897 ; in the Alabama State Asylum in Tuscaloosa (Alabama) in 1895 and 1896, and in the Arkansas State Asylum in Little Rock (Arkansas), in 1895. According to my knowledge, there are no exact statements as to the epidemics in Melton and Little Rock, so that no opinions can be given on these ; but of the epidemics in Sainte-Gemmes-sur-Loire and in Tuscaloosa, Chartemesse, Ramond,[1] Bondurant,[2] reports have been furnished. These reports, however, do not convince me that the disease in question was actually beri-beri. Both epidemics exhibited diverse symptoms, not quite characteristic of beri-beri. Thus in the epidemic of Sainte-Gemmes-sur-Loire there were disorders of the digestion at the commencement of the illness, trophic disorders, especially an erythema resembling pellagra, on the back, the face and backs of the hands, paralysis of the bladder and rectum. In the Tuscaloosa epidemic severe digestive disorders prevailed, with irritation of the kidneys, ataxic and trophic disorders.

The isolated cases of multiple neuritis observed by Orthmann (Grafenberg-Ludenberg) and Tippel (Altscherbitz) in German lunatic asylums—and which Norman likewise attributes to beri-beri — have as little to do with that disease as the sporadic or limited outbreaks of polyneuritis (such as observed by Eisenlohr in Hamburg, and Protopopow in Russia) that sometimes occur. I cannot agree with Bälz's far-fetched opinion of years ago that the sporadic cases of multiple neuritis occurring in Germany are neither more nor less than sporodic cases of beri-beri. According to my views the two diseases are related, but by no means identical ; they may stand to each other as does cholera nostras to cholera asiatica.

Finally, the *epidemic appearance of beri-beri* on *board ships* during their voyage in certain seas is to be considered. The disease is most frequently observed on Dutch men-of-war, cargo boats, and coasting vessels sailing in the Indian Ocean among the islands of the Malayan Archipelago ; it is observed next in frequency on English men-of-war and cargo boats in the Bay of Bengal and in other parts of the Indian Ocean ; it is also met with on French steamers that carry Indian coolies backwards and forwards to and from India or the West Coast of Africa to the French Colonies in America (Antilles, Cayenne). There are, besides, reports of the occurrence of beri-beri amongst crews in the Torres Straits, in the Persian Gulf, the Red Sea, on board Japanese men-of-war off the Japanese coast, and in the Pacific Ocean ; on Brazilian men-of-war during the war with Paraguay in the Atlantic Ocean. The disease

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[1] *Une épidémie de paralysie ascendante chez les aliénés rappelant le béri-béri. Ann. de l'Inst. Past.*, xii., 1898-9, p. 574.

[2] Rapport of thirteen cases of multiple neuritis occurring among insane patients, *New York Med. News*, October 3, 1896, p. 365 ; *New York Med. Journ.*, November 20, 27, 1897 ; Ref. January 2, 1895, 5, p. 492.

usually broke out amongst the crews after a voyage of from three to four months.

Stékoulis reports that beri-beri broke out on board a guard ship, that was built at Genoa ; seven months after leaving Bombay, the disease exhibited itself amongst the Indian crew in the Red Sea, though there were no other cases in that locality at the time.

ÆTIOLOGY.

Beri-beri is an infectious disease and not a mere disturbance of nutrition as it is erroneously considered to be by those who start from the standpoint that food consisting chiefly of rice and dried fish, such as is the national food in the beri-beri countries of East Asia, is insufficient. On this hypothesis, the disease is attributed to a scanty and faulty diet, lacking albumen and fat. The correctness of the statement that beri-beri is an infectious disease is corroborated by the following facts, on which different observers in diverse parts of the globe coincide :—

(1) *Strong, well-nourished young persons* are most frequently attacked by beri-beri, and are particularly liable to the severest form of the disease.

(2) Beri-beri has not only its definite geographical region of distribution, but even in beri-beri countries it does not occur everywhere, being mostly confined to certain narrow, sharply limited districts. As we observed above, the disease rages principally in tropical and sub-tropical districts. Within this region of distribution it occurs by predilection on the sea coast, along the banks of large rivers, and on the contiguous plains. It is less frequent in the interior, and still less so in mountainous regions, though even these are not quite free from the disease, as proved by its occurrence in Indian hill stations ; in Fort de Koch in Sumatra (which is the garrison at the greatest altitude in the Dutch Indies) ; in the Japanese province of Thinano, &c. Beri-beri is, moreover, principally a disease of large towns, usually the low-lying parts of the city being principally attacked. Occasionally certain centres and certain buildings are specially attacked, particularly jails, barracks, and hospitals, and sometimes the disease is even confined to certain spaces and storeys of these buildings.

(3) The seasons of the year, or rather the *conditions of the weather* occasioned by the seasons, exhibit a certain influence on the appearance of the disease ; the maximum of the frequency of the disease occurs during that season which is first of all distinguished by *great* moisture, and secondly by a high *temperature liable to many variations* (Hirsch.)

In the *tropics* (in the Malay Archipelago, in India, in Singapore), beri-beri mostly appears during the rainy season. In Brazil it rages during the hot and damp seasons, and disappears in winter In Japan illnesses due to beri-beri occur throughout the year, but the maximum of cases as a rule occur during the hottest month, July, which is preceded in June, by one of the two rainy seasons of the year, while the least frequency of the disease is usually observed in December. In temperate climates (Yezo, Dublin), most cases occur in July.

In damp years, beri-beri is particularly frequent and severe, and floods, according to the observations made in Atjeh, are followed by a considerable increase of the disease.

(4) During recent decades, beri-beri has attained a considerable distribution in tropical countries, as in Java, Japan and Brazil, without any change of food having taken place amongst the people, so that this reason cannot be made answerable for its appearance. In Atjeh, where the disease now rages severely, it was unknown before it was annexed to Holland.

According to observations made lately by Kohlbrugge in the Dutch-Indian army, beri-beri resembles other infectious diseases, inasmuch as it exhibits *periodical fluctuations*. Amongst the Europeans, the number of beri-beri illnesses in the years from 1873-1874, were fairly low, then suddenly rose, and from 1888 again sank, but until 1895 it nevertheless remained far higher than it was previous to 1884 ; it subsequently decreased somewhat in 1896, and in 1897 fell considerably. Amongst Asiatics, the number of cases increased earlier and diminished later. Thus it was only when the unknown factors, which caused the increase of the disease, had reached their maximum, that the Europeans were attacked. The decrease of the disease preceded all the measures planned to effect that end.

By all these facts it is strikingly proved that the actual and essential cause of disease cannot be sought in defective or scanty nutrition. Famine has existed in all possible forms, at all times, and on every portion of the surface of the globe, without ever having caused the development of beri-beri as a sequence (Hirsch). At the same time it is not disputed that under certain circumstances want of food, like any other weakening factor, may act as a *predisposing cause* in the outbreak of the disease.

Beri-beri decreased in an extraordinary manner in Japan, in the navy as well as in the army, after changing the food by replacing a portion of the rice with corn or bread, and simultaneously improving the general hygiene. It is however doubtful if the improved diet effected this change. As Bälz states, the decrease of the disease took place in all the barracks, although the food was purposely not changed simultaneously. Furthermore, the enlistment of recruits was postponed from May to December, so that young soldiers fresh to barrack life are not submitted to unaccustomed and fatiguing gymnastic and marching-exercises during the relaxing and enervating summer months, but commence drill during the relatively cool winter months, by which plan they are acclimatised to their new life by the time the summer sets in.

Amongst the native marines of the Dutch-Indian navy, van Leent and van der Elst found a marked decrease of cases of beri-beri after the men received European rations in 1874 ; while Weinkauf attributes the decrease less to the improved diet than to the improved hygienic condition of the men-of-war, and he asserts that amongst the soldiers and the prisoners no decrease in the number of cases resulted from improvement of the diet.

Eijkman has lately, through the medium of the *Archive der Bureaux der Marine und des Kolonial ministeriums*, reopened this question with renewed investigations, and the results attained by him lead to the conclusion that, according to his experience in the Dutch-Indian navy, there are no grounds for connecting beri-beri with diet. The natives, though they regularly received European rations, did not eat them but partook of rice, which the Europeans also consumed. The Europeans' diet was not altered, yet a decrease of beri-beri took place ; but from 1880, notwithstanding that the diet was still the same, the disease again increased considerably.

Brémaud and Laurent have recently again brought up *fat-lacking food* as a cause of beri-beri. They observed that epidemics repeatedly ceased when fats (pork) were freely given to the healthy. Brémaud observed an epidemic on a ship which was confined to the Mohammedans, who supplied their own food, which was non-fatty, while the rest of the crew, who ate food from the ship's kitchen, were not attacked.

It is certain that a *rice diet* cannot be considered as the cause of the disease, for beri-beri occurs in regions where rice is not eaten, as in Brazil, in the Moluccas, and in the Lingga Archipelago, where the population live on sago, fish and game (Fiebig), and where the disease was observed in Europeans who at that time had never eaten rice (Voorthuis).

Eijkman and Vorderman have recently again brought forward the etiological connection between rice and beri-beri, but from a different point of view, their opinion being that the *kind of rice diet* in use has a considerable influence on the occurrence of beri-beri. Eijkman observed that fowls in the laboratory fed with cooked rice were attacked with a disease resembling beri-beri, and, like it, attributable to polyneuritis. After a period of from three to four weeks, paralysis of the legs set in, then paralysis of the wings, and finally of the respiratory muscles, the birds dying after a short time. This observation induced numerous and very varied experiments, the results of which were as follows : After feeding with raw rice the disease also sets in, but not so soon, and it could also be originated by feeding with various kinds of starch-flours. It was

prevented, on the other hand, by feeding the fowls with cooked or uncooked rice covered entirely or partly with the husk; or when the bran from the inner husks that clings to the grains of rice was added to the rice or starch flour; or less certainly when a mixture, consisting of the coarse husks and the inner lining of the husks, were added to the food; moreover sick fowls recovered when they received this food. From these experiments Eijkman concludes that it must be the inner husk that protects the fowls from the disease and cures it. Besides fowls, the disease could also be induced in pigeons, but not in ducks, guinea-pigs, or monkeys.

Eijkman's opinion was, that beri-beri had some connection with the presence of starch. From this a poison is probably generated in the crop of fowls and pigeons where the food is kept some time, resulting in polyneuritis; in animals having no crop the disease does not develop. In the husk, particularly the inner husk, a material is contained which, directly or indirectly, renders this poison harmless. This material, though in considerably smaller quantities, is present in flesh, as proved by the fact that sick fowls fed with lean raw meat recovered. From this it is to be inferred that the material must be one of the normal constituents of the body of the fowl.

Though the polyneuritis of fowls may not be identical with beri-beri, Eijkman nevertheless believes that the means which served as a protection and remedy for the fowls, may also prove effective in curing beri-beri, and his views are supported by the results of the investigations made by Vorderman on the occurrence of beri-beri in the prisons of Java and Madura in 1895 and 1896. In many districts of Java, partly-husked rice represents the staple food of the population, and the food given in prisons is on the same principle. Vorderman's investigations led to the following results:—

(1) Out of fifty-one prisons in which peeled rice (*i.e.*, the inner husk entirely removed, or at least 75 per cent. of it taken away) is eaten, 36 = 70·6 per cent. contracted beri-beri in the proportion of 1 case beri-beri to 39 prisoners.

(2) Out of thirty-seven jails with half-husked rice (*i.e.*, the whole or 75 per cent. of the inner husk kept on) as staple food, 1 = 2·7 per cent. had beri-beri; 1 case beri-beri to 10,000 prisoners.

(3) Out of thirteen prisons with a mixture of half-shelled and shelled rice as staple diet 6 = 46·1 per cent. had beri-beri; 1 case to 416 prisoners.

In several prisons and hospitals in which Vorderman advised that rice with husks should be given, beri-beri ceased.

The results of Eijkman and Vorderman have undergone searching criticisms, especially from Glogner[1] and van Gorkom and, as a matter of fact, many exceptions can be taken to them. In Eijkman's experiments the objection is raised that he caused polyneuritis in fowls by means of various foods; that the neuritis only set in after a long period (six to seven months), and the favourable effect of the rice with husks was only exhibited after some time (six to eleven months) or did not appear at all; poultry fed with rice husks also fell ill. In addition, Eijkman's experiments were conducted in a very unhealthy locality, quite a number of his experimental animals dying from other diseases; the cause of the polyneuritis may therefore be attributed to a cause other than the feeding. Vorderman's observations extended only to one year or one year and a half, a time much too short to exclude the statistical errors that are apt to be made, and to confirm the genuineness of a certain phenomenon. As to the favourable results attained by giving rice with husks, these occurred simultaneously with the above-mentioned general decrease of beri-beri in the Dutch Indies. Van Gorkom even goes so far as to doubt Vorderman's statements. The prophylactic and therapeutic experiment of treatment by rice with the husks retained appears to have now been relinquished in the Dutch Indies.

Specific injurious substances contained in food are, by many persons, said to be the cause of beri-beri, but the positive proofs of this hypothesis are nevertheless lacking. Gelpke asserts that *very stale and badly kept rice* is the cause of beri-beri. Formerly the same author attributed the disease to a hypothetical *micro-parasite* resembling trichinæ, supposed to be contained in the *dried fish* used as food. Van Dieren and Yamageiva regard the illness as *rice-poisoning*. Le Roy de Méricourt identifies it with *lathyrism* (see lathyrism). Lately Miura throws the blame on the eating of the flesh of certain kinds of "scomberoids" as the cause of beri-beri, and Grimm also considers that the *eating of certain kinds of raw fish* causes the disease.

The above-mentioned statements, while declaring against the view that beri-beri is a disturbance of nutrition, seek to establish the fact that the disease is attributable to a specific cause originating outside the body, and that beri-beri therefore is to be regarded as an *infectious disease.* The analogy with *malaria* is, in some respects, striking, and therefore

[1] *Arch. für Schiffs- u. Tropen.-hyg.*, ii., 1898, pp. 39 & 40.

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beri-beri was formerly often regarded as being a peculiar form of malaria. This erroneous view is contradicted, however, by several important facts, above all, by the utterly different clinical and pathological features afforded by the two diseases, and their different geographical distribution.   On the one hand there are deadly malarial regions that are free from beri-beri, such as the province of Orissa, the Delta of the Ganges (India) and the notorious district, Tjilatjap, on the south coast of Java; on the other hand, beri-beri is endemic in many districts in which malaria is rare, such as Singapore, and the mountainous parts of several districts of the Malay peninsula.   Moreover, it must be borne in mind that beri-beri occurs in towns, malaria in the country, also that quinine has no effect whatever on beri-beri.

Glogner has lately attempted to ascribe at least a portion of the beri-beri illnesses to malaria. He communicates four cases in which, besides symptoms of beri-beri, malarial fever was present, aggravation of the former after the latter and *vice-versa* was observed, and malaria parasites were present. According to my opinion, however, these cases were complications of beri-beri with malaria.

I consider that there is no question of contagion in beri-beri.   In cases where several illnesses occur in one house, simultaneously or close one after the other, or where persons nursing beri-beri patients are attacked with the same disease, another explanation must be admitted.

On the other hand, it seems to me that the mechanical *transmission of the disease* through human intercourse is confirmed by the facts mentioned above, namely, that in recent years a spread of beri-beri has taken place in different countries—in Java, Sumatra, Japan, Brazil—with the increase of commerce, and, in addition, the epidemic appearance of the disease on ships or amongst the crews coming from beri-beri countries.   A few examples of the transmissibility of beri-beri are also contained in the literature on this subject.

Beri-beri, hitherto unknown in the Penang jail according to Grey, broke out soon after the importation of two hundred prisoners from Singapore, where the disease is endemic.

Vorderman communicates similar observations from the jails of the Dutch Indies. In Kraksäan, where hitherto beri-beri was unknown, it broke out under the following circumstances.   A number of prisoners, on account of the rebuilding of Kraksäan jail, were transported thence to Probollingo, where the disease is endemic.   When the prisoners returned to Kraksäan a few were suffering from beri-beri, and other prisoners also developed the disease.

Manson cites the following instance:—Eight hundred labourers from Tonquin and Annam were landed on the quarantine island of Freycinet.   After a short time beri-beri broke out amongst them and caused twenty-eight deaths.   The island was abandoned, and four hundred immigrants were landed at Koutia Koueta, 15 km. from Noumea.   Beri-beri persisted, forty of the four hundred died and the disease spread to neighbouring places and caused the death of ten of the labourers who had lived there previous to the arrival of the infected immigrants; persons from the Salomon Islands, and from New Caledonia and the New Hebrides, were attacked.

Macleod reports an interesting observation:—After a four months' uninterrupted voyage the captain and the three officers of the sailing-ship Ancona, which sailed from New York on August 19, 1896, fell ill from beri-beri in the vicinity of the Salomon Islands.   None of the men had ever been in a beri-beri country.   Two of the officers died, and on arrival of the ship in Shanghai on April 17, 1897, the captain and the surviving officer were still ill.   The hygienic conditions of the ship were good, and the crew remained healthy.   As the diet of the crew and officers was different, the latter besides tinned foods partaking of ham, bacon, sago, tapioca and arrowroot, Macleod considers the cause of the disease was attributable to the food, and is of opinion that the farinaceous foods, which came from beri-beri countries, were the carriers of the virus of disease.   Although the ship came from Australia (Melbourne), where beri-beri occurs, by Portland (Oregon) to New York, and the cook and steward on board were both Chinese, it is nevertheless highly probable that the virus of disease was carried into the ship by some other means, remained latent at first, and only developed

when exposed to climatic influences favourable to its growth in the vicinity of the Salomon Islands.

The *nature of the virus of the disease* is still unknown, at least my personal opinion is that the micro-organisms hitherto found in the blood and tissues of beri-beri patients by various observers, are not the specific excitants.

Quite a number of *bacteriological examinations* have been published, but the results differ so considerably one from the other, that it is impossible to find in one the confirmation of another's discoveries. Thus Lacerda discovered bacilli and cocci in the blood of beri-beri patients ; Ogata, bacilli ; Taylor, spores ; van Eecke, three species of cocci and one of bacilli ; Pekelharing and Winkler, cocci and bacilli of various kinds ; Musso and Morelli, four kinds of cocci ; and Nepveu, three kinds of bacilli.

The investigations of Pekelharing and Winkler have attracted the most attention, and the results, briefly given, are as follows : In their blood-cultivation experiments on 80 cases, they found in 65 cases no bacteria ; in 6 cases white cocci liquefying gelatine ; in 2 cases white, non-liquefying cocci ; in 2 cases yellow cocci ; in 2 cases other cocci not examined minutely ; and in 3 cases bacilli of various kinds. Their discoveries, therefore, were *very inconstant*, and in addition, the methods adopted in the greater part of their examinations faulty. They even consider the bacilli to be impurities. Experiments on animals conducted with these, as also with yellow cocci, gave negative results. Of twelve experiments conducted with the white liquefying cocci nine gave positive results ; of eight conducted with the white non-liquefying cocci three yielded positive results ; that is to say, degeneration of the fibres of certain nerves was discovered ; but this also frequently occurs under normal circumstances in the animals most frequently used for experiments, namely, rabbits, and most probably also in dogs and guinea pigs ; and as a matter of fact is most frequent in the nerves of the hind leg, which are usually used for the experiment. Pekelharing and Winkler in their experiments disregarded the other pathological, anatomical, and histological changes characteristic of beri-beri ; and also laid but little weight on the symptoms of disease exhibited by the animals experimented upon during life—two exhibited abscesses, two peritonitis, one purulent pleurisy.[1]

Although Pekelharing and Winkler's discoveries could not be confirmed by Eijkman and Sternberg, it ought to be mentioned that Hunter has lately in four cases found *staphylococci* in the blood (several times besides different bacilli), which he identifies with Pekelharing and Winkler's white cocci. These white cocci, injected repeatedly into the abdominal cavity of rabbits, caused paralysis, death and parenchymatous degeneration of the nerves of the hind-legs, and several times also small hepatic abscesses. He also found similar, but less virulent, cocci in the rice which two of the patients had eaten.

Lately Glogner, in a great number of cases of beri-beri which mostly ran their course with splenic enlargement and mild fever, found (but not constantly) *forms similar to* malaria parasites in the blood of the spleen ; the forms are mobile and pigmented, and increase by means of throwing off roundish marginal particles. They are distinguishable from malaria parasites by containing more pigment, by the circular arrangement of the same, and by its appearance being exclusively extra-globular and only limited to the splenic blood. In a few cases malaria parasites were simultaneously present. Glogner also found the same forms in various patients suffering from splenic enlargement and intermittent atypical fevers, without symptoms of beri-beri. Before being convinced to the contrary by illustrations of the forms described,[2] and by accurate temperature charts, both of which are missing in Glogner's publications, I am inclined to the belief that the cases in question are nothing but complications of beri-beri and malaria.

Fajardo and Voorthius respectively, found *hæmatozoa* in the blood, lying partly free, partly in the red blood corpuscles ; but these neither coincide in form one with the other, nor with those described by Glogner.

No observer, with the exception of Taylor (?), has hitherto succeeded in generating beri-beri in animals by means of freshly drawn blood from beri-beri patients. The blood, therefore, either does not contain the questionable ætiological factor of the disease, or the animals used for the experiments are immune from beri-beri.

[1] My monograph on beri-beri contains a detailed criticism on Pekelharing and Winkler's experiments, p. 188.

[2] *Remarks in the proof.*—The illustration of the excitants of beri-beri appearing in Glogner's latest work (*Virch. Arch.*, clviii., 1899, No. 3, p. 444), which are not stainable, impress me as being pigment.

Van der Scheer has recently drawn attention to the question that, as beri-beri is particularly a disease of dwellings, perhaps certain creatures living in houses, such as cockroaches, may play a part in its transmission.

Although the actual cause of beri-beri has not yet been discovered, we must picture it to ourselves as a tiny living being, be it of vegetable or animal nature, which, invading the body from outside either by means of the respiratory organs or the digestive canal, develops here, and originates the disease by the injurious effect of the poisonous products of its metabolism (ptomaine) on the nerve tissues. We know for a certainty that great moisture and a high temperature are necessary to its development, and that it has a certain connection with the *soil*. The soil, independent of its geological character—for the disease occurs on alluvial, volcanic, and rocky soil—is probably its original place of development. Disturbance of the soil favours the development of beri-beri as well as of malaria. According to the observations made in the tobacco plantations on the east coast of Sumatra, the disease occurs more frequently amongst the coolies on the newly opened plantations, than amongst those plantations that have existed over a year (Elsberger, Voorthius). In Japan it has been frequently observed that the inhabitants of newly-built-on, hitherto uninhabited, places, are apt to be visited by beri-beri during the first years. As we have seen, the germ of the disease is to a certain degree transmissible ; it therefore can be carried, not only from one place to another, but from the soil to buildings and to ships, and there, subject to its finding the conditions necessary to its development, *i.e.*, the needful damp and warmth besides a suitable nutritive soil, it may establish itself, multiply, and thus form fresh breeding places. Persons dwelling in buildings with damp foundations are particularly liable to be attacked. The transmission of the determining factor of the disease can of course take place by means of human beings, as well as by means of inanimate objects, such as clothes, &c.

Roll believes that the infection is distributed by means of drinking water. He reports two epidemics on board ship that broke out four or five weeks after shipping drinking water from beri-beri localities. As long as European drinking water was on board no cases of illness occurred, notwithstanding the stay of the ships at beri-beri localities.

According to Fiebig's opinion the questionable micro-organism does not itself invade the body, but stops in the soil and there generates a gaseous material (be this a product of metabolism of the microbe, an evanescent ptomaine, or be it formed by a specific fermentation excited by the microbes from some material in the soil) which rises from the soil and is taken up by the respiratory organs. The rise of the beri-beri gas, according to Fiebig, depends, like ebb and flow, on the rise of the atmospheric air, on the gases of the soil, the lava (Falb's theory of earthquakes) and on the position of the earth to the sun and moon. Beri-beri and the chart of the earthquakes in the Malay peninsula exhibit a fairly parallel course. In 1885 and 1886, in which years Atjeh was severely visited by beri-beri, most earthquakes also occurred. The rise and fall of the beri-beri chart in the course of the year is, according to Fiebig, caused by the sun's incidence.

I do not think it probable that beri-beri is originated by *different microbes*, and therefore does not represent a disease *per se*. Pekelharing and Winkler incline to this opinion, which has lately also been expressed by Glogner, who differentiates malarial beri-beri, dysenteric beri-beri, &c. Notwithstanding the manifold diversity of the separate cases of disease, the whole picture of disease gives me the impression that it is the question of one single disease, and not of a group of diseases, as is the case in the multiple neuritis occurring sporadically in Europe.

Race and *nationality* play an important part in the ætiology of beri-beri. In all those countries visited epidemically, or are endemically subject to the disease, and in which a mixed population lives, the *natives* and *immigrant coloured races* are principally attacked ; whereas the immigrant Europeans and North Americans enjoy an immunity which, if not

absolute, is nevertheless very marked, and is more pronounced in some countries than in others.

In regard to the immigrant coloured races, the condition of different races, as in the Chinese, vary in different countries ; in some countries they enjoy less immunity than in others. A few nations. like the people of Atjeh and the Ainos, do not develop the disease in their own countries, or are much more rarely attacked when at home than when abroad.

Besides the difference in race, the favourable *hygienic conditions* under which Europeans and Americans live in all these countries, have a great deal to do with their exemption from beri-beri. From this circumstance it appears to me, that the reason Europeans were formerly more liable to be seized with beri-beri than at the present time, is to be sought in the fact that formerly the hygienic conditions were not so good as now. At the present time soldiers, who are compelled to live in the same manner as the natives, are especially liable to beri-beri, while a case amongst the civilians is a great rarity.

According to reports from all beri-beri lands, the *male sex* exhibits a far greater predisposition to the disease than the female sex. The relative immunity of females, however, appears at least partly to be grounded on their manner of living, which in many respects differs from that of males. When females are exposed to similar conditions of life, the immunity decreases, as proved by the epidemics observed in orphanages, boarding schools and convents.

As to the *age*, beri-beri is mostly a disease of the *prime of life*. According to my observations, the ages from 16 to 25 years are most liable to the disease. The age of childhood, with few exceptions, is spared, and the disease is but seldom exhibited in extreme old age. My youngest patient was 8 years of age, my oldest 65.

Dr. Graham, of Deli, Sumatra, sent me the photograph of a Chinese boy, not 5 years old, who was suffering from dropsical atrophic beri-beri.

Hirota (Tokio), observed a peculiar feature of the disease in *children about one year old*, who were being suckled by mothers or nurses suffering from beri-beri. The infants were restless, and suffered from vomiting (seldom from diarrhœa), had deep aphonic voice, cyanosis (round the mouth and nose), soft, rapid pulse, increased cardiac action, augmented second pulmonary sound, occasionally cardiac dulness extending to the right, acceleration of the respiration, decrease in the quantity of urine, and œdema. In most cases, change of nutrition ensures rapid improvement and recovery. In a few cases death ensued notwithstanding change of food. Hirota identifies this disease with the acute, severe beri-beri of adults, and believes it to be due to intoxication caused by the milk of the women suffering from beri-beri. That he was unable to confirm any symptoms of paralysis is explained by Hirota by the fact that slight motor and sensory disturbances easily escape observation in sucklings ; but none of the pathological and histological changes characteristic of beri-beri, more especially the disease of the peripheral nerves, have been confirmed. Hirota communicates the result of one *post mortem*, Miura of four, in all of which there is no mention of the nerves. In four of these cases catarrhal pneumonia was doubtless the principal ailment. Miura lays great stress on the hypertrophy of the right ventricle that was exhibited ; this. however, is nothing but a physiological appearance. It is known that during the fœtal life there is no essential difference in the thickness of the walls of the two ventricles. which only gradually form during life, and is therefore not yet very pronounced in sucklings. After all said and done, I am not convinced of the existence of infant beri-beri.

The *constitution* has a marked influence in beri-beri. According to the experience of medical men in the different beri beri lands, strong persons are attacked by the disease far more frequently than weaklings. At the same time the predisposition to the disease may be increased, as we shall see below, by previous exhausting illnesses.

As to *position* and *occupation*, beri-beri, according to the observations

made in Japan, occurs principally amongst the middle classes. It decidedly
appears less frequently in the lowest strata of the population, but it does
not spare those in high or in the highest positions. Those most frequently
attacked are, on the one hand, soldiers and prisoners, on the other
hand, amongst civilians, it occurs in persons whose occupations necessitate
a sitting posture. By far the largest contingent of my patients consisted
of teachers, students, priests, clerks, merchants, shopmen, artists and
artisans. Similar observations have been made in Brazil. The reports
from Dutch and British India principally relate to soldiers, sailors and
prisoners, but this is attributable to other conditions. Fiebig, lately,
has pointed out that beri-beri occurs far more frequently than hitherto
supposed amongst the native population, and in the coloured people who
are not exposed to compulsory labour, nor to a sedentary manner of
life; and that principally fishermen, hunters, sago-gatherers, gardeners
and pearl fishers are attacked, none of whom pursue their calling in a
sitting posture. As to the sitting posture, the lack of bodily movement
can hardly be considered an ætiological factor, as soldiers and sailors, who
are so often attacked, do not lack exercise. It is more reasonable to
suppose that *continued dwelling in a more or less crowded, badly-
ventilated apartment* may have some influence (Hirsch); for that, in con-
junction with other unfavourable hygienic conditions is, according to
the opinion of many observers, of great influence in the genesis of beri-
beri. The justice of this view is proved by the remarkable frequency
of the appearance of the disease in *barracks, prisons, asylums, factories*
and *ships*. On board ships, beri-beri has been observed to break out
principally when, in consequence of stormy weather, the holds, &c., have
had to be kept closed. According to Pekelharing and Winkler, the micro-
organism always finds nourishment where it can reside and multiply in
buildings, &c., in which many persons live together.

Swäving, Bälz, and Ten Bosch, lay particular stress on the *sleeping together of
several persons* in small apartments. As Bälz observes, soldiers, students, &c., fell ill
more frequently than factory hands, although the former have more fresh air in the
day time than the latter.

According to Fiebig (see above, p. 196) the exterior pressure on the nocturnal
part of the globe is less than on the matutinal side, because the hemisphere turned
from the sun is subject to a greater tangential rapidity than the hemisphere turned
towards the sun. Therefore, during the night, there is a greater rise of gases from
the soil, and the beri-beri gases rising at the same time (earthquakes are also more
frequent at night), the symptoms of disease in beri-beri are correspondingly aggravated
during the night, so that the patients first remark them either during the night or on
rising early in the morning.

All the lowering factors, which become pre-disposing causes in other
diseases, are given as incidental causes of beri-beri. They consist of chills,
wettings, bodily and mental exertions, emotion, and excesses of all kinds.
Mirando Azevado considers that sleeping in the open air is a predisposing
cause. Rupert is of opinion that the disease is caused by sleeping on a
level with the soil, and Elsberger by working on marshy ground. My
patients most frequently asserted that long marches were the incidental
causes. In women, pregnancy, confinement and suckling are predisposing
causes, and the same consequences result from the weakening influence of
other diseases. As a rule beri-beri develops during the course of, or in
addition to, acute diseases. Beri-beri has been observed by me second-
arily, especially during or after typhoid fever, cholera, dysentery, malaria,
acute articular rheumatism, catarrhal diseases, pleurisy, and also in
syphilis, in pulmonary and laryngeal phthisis, and after operations.
In women, according to Féris, severe menorrhagia leading to anæmia
frequently predisposes to beri-beri.

The same influences that serve as incidental or exciting causes may also cause the aggravation of symptoms when the disease is present   Nevertheless it is sometimes observed that when during the course of beri-beri other diseases occur intercurrently, which is often the case, there is an improvement in the beri-beri.

Finally, *acclimatisation* is of importance.   In places where beri-beri is endemic the natives are attacked by the disease far more rarely than those who have immigrated from elsewhere ; immigrants, however, only become affected after a long stay in a beri-beri district, and this holds good not only for foreigners but for persons belonging to the same country and nation.   According to my observations, the circumstance of beri-beri being endemic in the home the immigrants have left has no influence.   The time that elapses between the period of immigration and the period of acclimatisation varies ; according to my experience it fluctuates between weeks, months, and years ; a period of over six months, however, is the rule, and in this connection much depends on the season during which the immigration into the beri-beri district has taken place.

The predisposition is not extinguished by recovery from the disease ; on the other hand, he who has once had beri-beri is apt to be attacked again.   The *relapses* are sometimes milder, sometimes more severe than the initial attack, and are repeated every year for shorter or longer periods, sometimes ten, twenty, or even thirty years, the attacks meanwhile becoming milder and milder, until finally the victims may be regarded as immune.   Sometimes the disease remains absent for one or several years, and then appears anew.   Occasionally two, or even three, attacks occur during the course of one year.

According to an old statement of Schneider, which, however, requires renewed confirmation, beri-beri very often occurs amongst animals ; fowls, sheep, oxen, horses, dogs and pigs being liable to it.   De Lacerda declares that the horse-disease " quabra banda " (plague of horses) prevailing in Marajó Island (Brazil) is identical with beri-beri.

SYMPTOMATOLOGY.

Beri-beri may exhibit several different clinical aspects.   At one time the symptoms caused by the disease are so trivial, and the condition of the patient so little disturbed, that one is hardly inclined to consider him ill.   In other cases the patients exhibit the most serious disturbances, and the disease may tend to a fatal termination with a rapidity observed in but few other diseases.   In both instances, however, the same disorder is present ; in both the same symptoms of disease are observed, only the degree of their development is different.   These differences in the features of the disease have led to the recognition of several *forms* of beri-beri, although these cannot be sharply differentiated one from the other ; the most manifold transitions from one group to the other occurring.   I consider it practical to differentiate the four following forms, as I have already done in my previous publications.

(1) The incompletely developed or rudimentary form.—The disease as a rule commences so imperceptibly that the patient is unable to mention a certain day on which the illness began.   Its outbreak, however, as in the other forms, may be preceded by a *prodromal* stage, lasting several days, or even weeks, and is characterised by general but indefinable indisposition or by rigors, disinclination for work, low spirits, headaches or heaviness of the head.   I, myself, have but rarely observed such a prodromal stage.

I observed more frequently that the outbreak of the disease was preceded by catarrhal symptoms, accompanied at first by feverishness. Sometimes the illness was ushered in with a cold in the head or a bronchial catarrh, sometimes by gastric catarrh or muco-enteritis.

The first symptoms are languor and a feeling of weight in the legs. The patients feel weak in the legs and walking tires them quickly; they complain of looseness of the knee-joints, tension in the calves when walking, and occasionally movement induces pains in the legs. Simultaneously, or soon after—or this may be the first symptom—the patients observe a slight diminution of sensibility in the legs; on touching anything they have a feeling as if a piece of paper, or something of the sort, had been pushed between the leg and the article touched. This diminution of feeling is at first confined to a circumscribed spot and is frequently accompanied by sensations. Œdema of the legs accompanies these symptoms; it does not as a rule amount to more than a slight degree, but often changes in severity, and is mostly only of short duration. The symptoms gradually increase, and the numbness extends slowly to other parts of the body. After some time palpitation of the heart usually sets in; sometimes, indeed, this forms the patients' first complaint. At first it is only slight, and is only apparent on active exertion; little by little it becomes more troublesome, and in course of time appears when resting. The patients, moreover, complain of oppression, most of all of pressure over the pit of the stomach. More rarely there is shortness of breath. The digestion is frequently disordered. The general condition, as a rule, is disturbed and the spirits low. These symptoms, however, are by no means constant.

It is in this stage that the patients usually seek medical advice. The objective symptoms exhibited are mostly the following: Diminution of the gross strength of the legs and in a less degree of the arms, more or less extensive slight anæsthesia of the skin, sensitiveness of certain muscles on pressure, particularly of the calves; certain changes of the heart to be more minutely gone into later, and more or less pronounced anæmia, which is frequent but by no means constant.

The condition of the patients may remain the same for months. Then, especially on the appearance of the cold season, improvement sets in and recovery ensues.

The development of every symptom here quoted does not take place in all cases. In the very mildest cases there is occasionally but one or other symptom, such as weakness of the legs or tension in the calves of the legs, and a diminution of sensation, &c.

The duration of the disease in this form may be a few days or several months, but cases also occur in which it lasts for years, becoming, as it were, habitual. Occasionally in such patients an aggravation of the symptoms occur in the warm season and a diminution of the same in the cold season. One of my patients had been suffering from beri-beri for twenty years.

(2) The atrophic form.—The atrophic form, like the rudimentary form, may set in insidiously with languor, weakness and heaviness of the legs, and tension in the calves when walking. The powerlessness of the legs gradually increases and the arms likewise become weak and paretic. Finally, the patients are no longer capable of walking and become permanently bedridden.

In other cases the paralysis develops quickly, within a few days, and it may even set in suddenly like a stroke.

As a rule the paralysis is confined to the limbs and trunk, but in
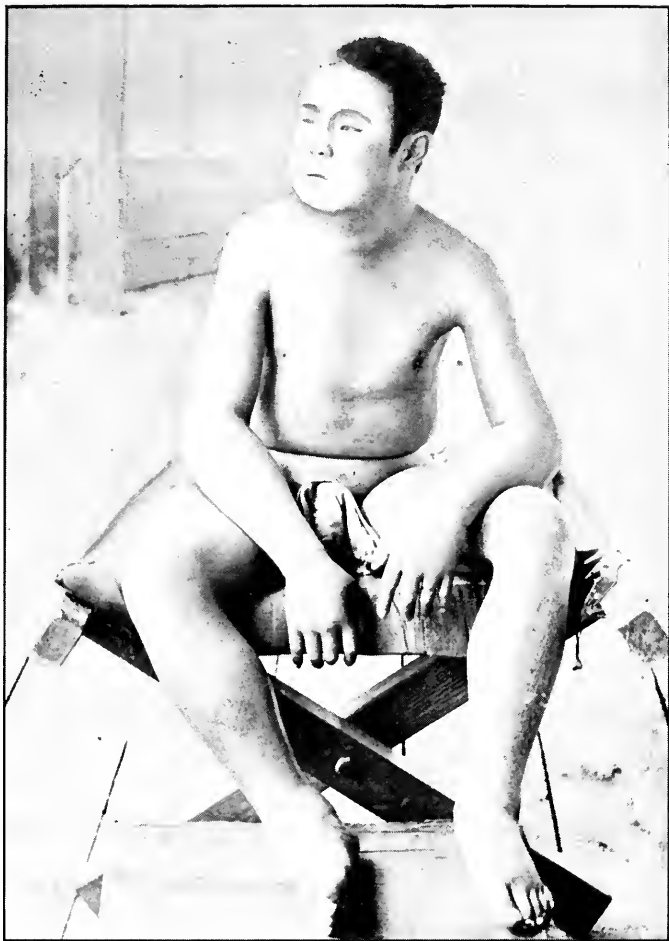
BERI-BERI: Œdematous variety.   Japanese immigrant in Fiji.

BERI-BERI; Atrophic variety, showing Muscular Atrophy and Drop-wrist.
Japanese immigrant in Fiji.   Photographs by HENRY NOBLE JOYNT, Labosa, Fiji.

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exceptional cases it invades the face, tongue, pharynx and larynx. In the severest cases the patients lie, a picture of misery, almost motionless, and entirely dependent on the help of those around them. In addition their limbs are at times so sensitive that the patient screams with pain at the lightest touch, and cannot even bear the pressure of the bed clothes. Sometimes they are also tortured by spontaneous pains; the paralysed limbs become excessively emaciated, the calves disappearing entirely. Sensation is disturbed to a greater degree than in the rudimentary form, both as regards the extent and also the grade of diminution of sensation; yet complete anæsthesia does not occur even in this form. On the other hand, cardiac symptoms and œdema are either entirely absent or only play a small part in the clinical features of the disease.

Recovery ensues very slowly; months generally elapse before the patient gradually learns to use his limbs again, and a year or more passes before they regain their former strength and contour.

In other cases, particularly those that are complicated with other diseases, such as typhoid, dysentery, pulmonary phthisis, &c., the illness takes an unfavourable turn. The weakness and exhaustion of the patients increase more and more, and towards the end of life œdema sets in; terminal complications, such as pleurisy, endocarditis, may ensue, consciousness is lost and death occurs quietly.

(3) The dropsical or moist, or hydro-atrophic, form.

This form is distinguished from the preceding by the appearance of *cardiac symptoms* and serous *exudations*. In isolated cases this variety develops from the atrophic form. As a rule the commencement is similar to that of the rudimentary form. The weakness of the limbs increases, sometimes quickly, sometimes more slowly; the patients can no longer walk. Generally, however, the paralysis is not to such a degree as is the case in the atrophic form. Moreover, the œdema does not remain confined to the legs, but gradually spreads over a more or less large portion of the body. In addition there are effusions into the serous cavities, palpitation of the heart, shortness of breath, oppression and pressure at the pit of the stomach attain a considerable hold; the secretion of urine is diminished. The disease may remain in this stage for weeks, the symptoms alternately increasing and diminishing. The absorption of the serous exudations ensues, with an enormous secretion of urine; the thoracic symptoms gradually disappear, and the general condition of the patients improves considerably. Only after the disappearance of the œdema does the emaciation of the paralysed limbs become apparent.

Occasionally the paralyses make further inroads, while the other symptoms abate. The reverse also sometimes occurs. The return of power to move comes slowly as in the atrophic form. As, however, the paralyses as a rule are not so considerable as in the atrophic form—sometimes being quite minor—recovery does not take so long, though from the time the patient was taken ill until recovery, nine months or more may elapse.

In 1877-1880 a disease bearing some similitude to the dropsical form of beri-beri, appeared epidemically in various districts of India, especially Calcutta, and in Mauritius, where it was probably imported from Calcutta. It was designated *epidemic dropsy*, or *acute anæmic dropsy*.[1] It was particularly distinguished by œdema, mostly of the lower extremities, which symptom was often preceded by vomiting, diarrhœa, pains in the epigastrium or abdomen, pains and paræsthesia of the limbs, accompanied in the

[1] K. Macleod, *Transactions of the Epidemic Society of London*, N. S., vol. xii., p. 55; "Allbutt's System of Medicine," vol. ii., 1897, p. 475; A. Davidson, *Edinb. Med. Journ.*, August, 1881.

severest cases by dropsy of the cavities and cardiac symptoms. There was, besides, marked anæmia, emaciation and prostration and frequent mild fever. Occasionally an exanthem supervened which consisted of a partly diffuse, partly spotty redness and was followed by petechiæ vesicles and desquamation. Occasionally also scorbutic and exceptionally doubtful paretic symptoms were observed. The duration of the disease was from three weeks to three months and the mortality varied between 2 per cent. and 40 per cent. Indians were principally attacked, and men more frequently than women and children. In India this disease prevailed during the cold and dry season, while in Mauritius it appeared independently of meteorological condition. No decided opinion is expressed in the reports as to the nature of the disease. Though there was an apparent absence of motor disturbances, and in spite of the appearance of the exanthem being observed in Mauritius more frequently than in India, it appears to me that it was possibly beri-beri. There are no later reports of this disease.

(4) The acute, pernicious, or cardiac form.

This form, which by predilection attacks persons in the prime of life, is characterised by symptoms of *acute cardiac insufficiency*, which may appear suddenly during the course of cases which previously appeared quite mild. More frequently, however, the entire course of the disease is acute from the commencement. Fatigue and heaviness in the legs, tension in the calves, diminution of sensation, slight œdema, palpitation of the heart and oppression occur in rapid succession and soon increase. After only a few days the paralysis of the legs may be so advanced that the patients are bedridden. In some cases, on the other hand, the paralysis does not attain so great a degree during the entire illness, and even very acute cases may run their course without either motor or sensory disturbances (Fiebig, A. Plehn). Early in the disease the cardiac symptoms become prominent. Palpitation of the heart, oppression and shortness of breath are the most troublesome symptoms. The appetite is usually lost soon after the commencement of the illness, and on the other hand the patients are tormented by unceasing thirst. The diminution of the urinary secretion is considerable, even at an early date. The œdema may be of only small degree or may even be absent. Accumulations of fluid are generally extant in the pericardium and other serous cavities, but as a rule the effusions are not so copious as in the dropsical form. Palpitation of the heart and dyspnœa steadily increase, the oppression sometimes rises to terrible precordial agony, the patient feeling as if his chest were being burst from inside. The urinary secretion decreases still further. Nausea and vomiting frequently set in. The patient's condition becomes more distressing and hopeless. He throws himself restlessly from side to side; his eyes, mouth and nostrils are wide open, the gaze staring and anxious, the pupils dilated. The carotids palpitate, the chest heaves continuously and violent palpitations, extending over the cardiac region and the pit of the stomach, cause great distress. The pulse in the meantime becomes smaller and smaller and finally is imperceptible. The face, before pale, becomes cyanotic, the limbs become cold, the temperature falls, the patient becomes unconscious, a frothy fluid issues from his mouth and a few moments after death ensues.

These symptoms of acute cardiac insufficiency sometimes drag on for a few days and sometimes cause death within a few hours. In the Dutch Indies it has been observed that native soldiers who had done duty in the morning, have succumbed to beri-beri by the evening, and that prisoners who had been regarded as malingerers, and therefore left in jail, have been found dead on the following morning ; A. Plehn has also reported on cases from Cameroon which ended fatally in from twelve to twenty-four hours. According to my experience, these very acute cases do not occur in Japan ; though it may be taken for granted that in such cases symptoms were present for a shorter or longer period, but had been

neglected on account of their triviality. In the cases observed by me, a week or two or a month elapsed between the commencement of the attack and its fatal termination.

Still another form, the *polysarcous* or *adipose*, has been described by Oudenhoven and by him alone. This form is characterised by hypertrophy of the adipose tissue, increase in bulk of the muscles, hypertrophy of the heart, the sudden appearance of œdema and serous effusions with some motor and sensory disturbances. Probably in this form it is the question of naturally fat persons (Thurm) ; or, as Le Roy de Méricourt conjectures, Oudenhoven has mistaken a solid œdema for fat.

The *convulsive form* of Vinson and van Overbeek de Meijer will be considered later on.

Grimm distinguishes two forms on the assumption that the exacerbations and relapses of beri-beri taking place during the attack are always fresh illnesses induced by repeated infection by the virus, while an uncomplicated case, running its course with final recovery and without any aggravation of the symptoms, is caused by a single infection.

(1) *Beri-beri simplex*, a simple attack of beri-beri induced by one introduction of the virus, and,

(2) *Beri-beri multiplicatum s. accumulatum*, which ensues in consequence of fresh infection of the virus again and again ; this is a division which is not worthy of theoretical recognition.

Yamagiwa, who attributes beri-beri to a poison ingested with food (rice), is of opinion that the virus causes a condition of contraction of the finer arterioles in the large and small circulation. This observer differentiates three forms : —

(1) The *cardiac form* (the most acute form) ;

(2) The *nervous-muscular form* (which is usually sub-acute or chronic, and accompanied by motor and sensory disorders) and,

(3) The *renal form* (dropsical form) varies according as the finer arterial branches of the lungs (cardiac form), or the arteries of the peripheral nerves and muscles (nervous-muscular form), or, finally, the branches of the arteries of the kidneys (renal form) are particularly attacked.

The relative frequency of the different forms of the disease differs in the various beri-beri countries. In some places the serious forms are more frequent than in others. Thus, in the Malay peninsula, the disease is decidedly of a more malignant character than in Japan. There is also a difference in different places in the same country. The frequency of the various forms may change in different years without apparent reason. It will therefore be seen that there are both periodical and local differences in the symptomatology.

Analysis of the Separate Symptoms.

(1) *Nervous system.—A disturbance of movement* is the most striking and constant symptom of beri-beri. This begins in the legs, and continues in the arms and other parts of the body, but is always most pronounced in the legs. The degree of this disturbance is remarkably varied ; all transitions occurring, from the mildest paresis only observable by the patient himself, to complete paralysis.

In the mildest cases the patients complain of languor, and weakness and heaviness of the legs. Walking is an effort, they soon become fatigued, the knee-joint or even the whole of the legs and feet feel loose, and sometimes in walking their knees knock together. Objectively also, with the exception of the earliest stages and the mildest forms, a distinct diminution of movement is observable in the legs. The gait, however, at this stage, exhibits no abnormality, and no complaints as to the arms are expressed as a rule. The examination with the dynamometer, however, mostly proves that in the arms also the gross strength is diminished, though it may be to a lesser degree.

When the paralysis has progressed still further, attention is directed to the patients by their unique gait, which has been appropriately compared (van Overbeek de Meijer) to the walk of a person emerging from the water with wet clothes on, or to that of somebody wading in stiff clay (Elsberger). The sole of the foot seems glued to the ground. The patient raises the foot with difficulty, shoots it forward, and then sets it down with a stamp. The steps, meanwhile, are very short and the legs are straddled in order to give a wider basis. One also occasionally becomes aware of a slight trembling. Those who wear sandals which are kept on by the toes, as for instance the Japanese, frequently lose them in walking in consequence of the disturbance of action in the toes, nor can they put them on again without the assistance of the hands. The hands also at this stage are often no longer able to grasp and hold things.

In cases still further advanced the patients are unable to walk and to stand, or to exercise the slightest pressure with the hands; but in the recumbent position they are still able to make a few movements. As a rule the extensors of both arms and legs are paralysed to a greater degree than the flexors, the paralysis mostly increasing in intensity from above downwards. In consequence of the ascendancy of the flexors, the hands and fingers remain in a bent position and the feet in the equino-varus position.

In the highest degree of paralysis the motor power of the limbs is almost completely suspended, such patients lying quite helpless and unable to move even a finger or toe.

Sometimes the paralysis is more pronounced on one half of the body than on the other, and I have even observed it on one side only.

If the paralysis of the arms and legs attains a high degree, the *muscles of the trunk*, more especially those of the abdomen, are apt to be more or less affected. The patients are incapable whilst lying to raise their head or upper part of body, nor can they raise themselves in bed without assistance; the respiration and reflex actions in connection with the same, such as coughing, sneezing, &c., are rendered more difficult, and evacuation at stool is hampered.

In severe cases paralysis of the *diaphragm* often occurs, when one observes that with each inspiration the pit of the stomach with the hypochondria are drawn in; the high position of the diaphragm can be confirmed by percussion.

The *phenomenon of the diaphragm* described by Miura (1891) is identical with the description given by Litten (1892).

The movements of the neck and head are not, as a rule, affected.

The cardiac branches of the vagus and the *motor cerebral nerves* are almost always attacked : acceleration of the pulse (see below) is one of the most invariable symptoms of beri-beri. Less frequently there is paralysis of the *laryngeal nerves* and, in consequence, the voice becomes hoarse and weak, or is quite lost. The *retching* and *vomiting*, which set in particularly frequently in the acute cases with fatal terminations, are probably attributable to irritation of the vagus nerve.

The *acute inflation of the lungs* to which I was the first to direct attention, is a further symptom which is frequently observed in the acute pernicious form ; according to Fiebig, however, it also occurs transiently in milder cases ; it is attributable to a paralysis of the *pulmonary* branches of the vagus.

With the increase of the subjective disorders the cardiac dulness becomes smaller and may disappear entirely within a few days, the

lower borders of the lungs move downwards, and loud resonance on percussion is occasionally heard over the lungs. I have only in rare cases found other cerebral nerves affected. In such cases, double-sided facial paresis, especially of the muscles at the angles of the mouth; dysphagia, difficult, tremulous movements of the tongue and disorders of articulation were the more prominent symptoms met with.

Da Silva Lima, as well as Pekelharing and Winkler, have exceptionally also observed paralysis of the muscles of the eye. One of Norman's patients (Dublin) exhibited ptosis, external strabismus, and dilation of the pupil of one eye.

Ataxia, according to my experience, does not occur in beri-beri, but on the other hand, there is instability on turning sharply round and when standing with the eyes closed, even in cases in which at the time there is no longer any loss of sensation. Elsberger observed the instability very often in the very first stage of the disease, so that he regards it as pathognomic.

The paralyses in beri-beri are as a rule associated with relaxed muscles; *tension of the muscles* are only exceptionally observed, and according to my experience, almost only on the flexor side of the leg.

In rare cases, which generally belong to the atrophic form, a *spastic contraction of the muscles of the calves* develops gradually during convalescence. Consequently, when the patients have regained the use of their legs and can walk, a characteristic form of gait is exhibited, resembling the walk in spastic spinal paralysis, the patients being only able to touch the ground with the ball of the foot. The muscles of the calves, especially the inner head of the gastrocnemius, may be hypertrophic, swollen and elastic to the touch, and the tendo-Achilles thickened. More frequently the contraction is accompanied by marked emaciation and induration of the gastrocnemius (see below). The muscles of the calves are in addition mostly tender to pressure, and each extension of the shortened tendo-Achilles may be so painful that the patients, who, in other respects, have complete power over their limbs, do not care either to stand or walk. The contraction of the muscles of the calves is generally a very tedious ailment, and in some cases may perhaps never entirely disappear.

In many patients *tonic convulsions* occur. Painful *cramps of the calves* are most frequent; they mostly set in during the night, and sometimes precede the usual beri-beri symptoms by a week or two. Extensive tonic cramps are of rare occurrence.

The following clonic forms of spasm have in rare cases been observed: Tremors, twitchings, involuntary movements, chorea or athetosis-like movements, or movements resembling those of paralysis agitans, and finally epileptiform convulsions extending more or less over the whole body are observed, especially shortly before death.

The occurrence of extensive tonic and clonic spasms has led to the setting up of the above-mentioned *convulsive or spasmodic form* of the disease.

The epidemics observed by Vinson on the Island of Réunion, and which commenced with high fever and violent spasm, belong to this form.

Fibrillar muscular twitchings are frequently seen in the affected muscles.

As to the *electric condition of the motor system,* the direct as well as the indirect *galvanic stimulation* of the affected muscles is more or less diminished even in mild cases of the rudimentary form. Frequently this

diminution of the muscular reaction is exhibited particularly, at times solely, by the gastrocnemius. During the further course of the disease the galvanic stimulation of the muscles decreases more and more with the degree of paralysis and atrophy; the indirect stimulation more than the direct, and at a high degree of paralysis it may be completely extinguished. Occasionally also isolated muscles, most frequently the muscles of the calves, exhibit qualitative changes in the form of spasm (sluggish, long-drawn contraction, A S Z > K S Z); the excitability, however, is mostly not in the meantime increased thereby, but diminished, and with faradic excitability completely extinguished.

When the general condition begins to improve, the excitability, *i.e.*, the normal manner of reaction, usually returns, but more slowly than the movement, so that while the muscles are again acting and have considerably increased in circumference, the excitability is still more or less diminished.

The *faradic stimulation* of the nerves and muscles diminishes more rapidly and is sooner lost than the galvanic stimulation, and the return to normal ensues later and more slowly.

Pekelharing and Winkler found that the electrical phenomena are the earliest objective symptoms, and precede the disturbances of movement and sensation. This observation, which would be of the utmost importance in the diagnosis of doubtful cases, has not been confirmed. In the East Indies the experience was that electrical abnormalities might be absent in well-confirmed cases (Eijkman, Glogner, Fiebig). It therefore seems that the quantitative deviations only become recognisable when they far exceed the normal degree of excitability which, in themselves, differ much.

According to Glogner, the electrical excitability of the nerves on different days is subject to more considerable fluctuations than normal; with the decrease of the same, an increase of the frequency of the pulse often sets in.

The *mechanical excitability* of the muscles, according to my observations, decreases with the increase of the paralysis, but continues longer than the electrical excitability. Pekelharing and Winkler often found it heightened with simultaneous rise of the galvanic excitability.

The motor disturbances are connected with the disturbances of sensation.

The appearance of more or less extensive cutaneous anæsthesia or actual cutaneous hyperæsthesia are the most constant symptoms. Sensation, as a rule, is only diminished to a slight degree; there is never a complete cessation of feeling. Hyperæsthesia is not limited to the regions of ramification of certain nerves. In accordance with my observations it generally commences symmetrically on a circumscribed spot of the legs and feet, as for instance on the inner surface of the legs, on the calves, or on the toes or dorsum of the foot. During the further course of the disease it extends, often very quickly, over a larger or smaller part of the legs, becoming more pronounced on the places that were first attacked; then as a rule the arms, commencing with the finger tips, are affected in their turn. Moreover the trunk, neck and face may be attacked; in the face the muscles round the mouth are especially liable to be attacked, the hyperæsthesia, otherwise, not being extensive. Norman, in a few cases, observed anæsthesia of the pharynx. As a rule the hyperæsthesia gathers in intensity from above downwards; on the limbs it is usually more severe on the extensors than on the flexors. The soles of the feet usually remain normal. On the forearms and hands the radial side is by predilection the seat of the hyperæsthesia.

In some cases the hyperæsthesia does not start in the legs, but in other parts of the body, such as the tips of the fingers, the abdomen, &c.

Occasionally its spread on the two sides of the body is not symmetrical, and it may even be confined to one side.

Occasionally, mostly at the beginning of the illness, or after convalescence has set in, the hyperæsthesia is not continuously present but only appears periodically, and principally in the morning.

In fact the other symptoms, such as the fatigue of the legs, the palpitation, and even the œdema, are often apt to be more pronounced in the morning than during any other time of the day (see above, p. 198).

Moreover, the weather and bodily movements influence the hyperæsthesia as it increases after motion, and in cold, and especially in wet and cold, weather. The general condition of beri-beri patients is, however, in other respects better on cold than on hot days.

The severity of the attack, the motor disturbances and the extent and severity of the hyperæsthesia by no means always run parallel; in mild cases it frequently happens that a large portion of the surface of the body is hyperæsthetic, while in serious cases, on the other hand, only quite small spots may be affected.

I observed the highest degree of lessened sensation in patients suffering from the atrophic form.

Frequently the hyperæsthesia is the first symptom of beri-beri and sometimes it sets in remarkably late. Sensation as a rule returns to the normal state earlier than the motor disturbances.

In a few of Norman's patients *anæsthesia dolorosa* existed; although sensation was diminished the slightest touch elicited pain.

As to the different *qualities of sensation*, I found these disturbed in a very unequal manner in different patients, as also in different parts of the body of the same patient. It is therefore not surprising that the statements of the various observers differ one from the other. Besides the diminution of the *sense of touch* to which the above remarks apply, I was able, most frequently, to demonstrate a decrease of the sense of *locality* and *pressure*. The sense of *temperature*, according to my experience, is but seldom materially disturbed; and the sense of *pain*, also, is retained for a fairly long time. I likewise found the *Farado-cutaneous sensation* diminished, occasionally to a far higher degree than the other qualities of sensation. I have never observed disorders of muscular sense.

I could only exceptionally confirm a retardation of the conduction of sensation.

Hyperæsthesia, general as well as circumscribed, is a rare phenomenon, according to my observations. Norman often found an area of hyperæsthesia round each zone of anæsthesia.

Paræsthesia, on the other hand, is remarkably frequent and of great diversity, and may precede the other symptoms of disease. The legs are their particular seat, and the weakness of the legs which forms so constant a complaint of beri-beri patients, is no doubt, at all events partly, to be attributed to paræsthesia. The following paræsthesiæ are, moreover, frequently observed : A feeling of tension that is most frequently exhibited on the calves of the legs and may, not rarely, increase to actual pain; a sense of dragging in the popliteal space; with it may be numbness, pins and needles, smarting, burning, formication, vermication, itching. More rarely there is a sensation as if the entire body or a part of it were swollen or thickened, a feeling of stiffness, subjective sensations of temperature (cold, heat). In a few cases I have observed sensations similar to globus hystericus and a kind of sense of constriction.

Like the hyperæsthesiæ the paræsthesiæ are also affected by the weather, being originated by wet or cold weather. Cold water or a cold wind may have the same effect.

Pains are not so frequent in beri-beri as paræsthesiæ, but they occur on the most different parts of the body ; they are, however, most frequent

in the calves of the legs and may be of the most manifold description (pricking, pressing, dragging, cutting, dull, flying). I have also frequently observed intercostal neuralgia and articular pains. A few of Norman's patients complained of burning pains in the soles of the feet. Däubler [1] saw patients who were tortured by such excruciating pains in the whole body, especially in the abdomen, that they screamed dreadfully, more particularly at night.

Sensitiveness or painfulness of isolated spinous processes is frequently exhibited on palpation with the percussion hammer, more especially in those of the upper dorsal vertebræ ; occasionally also this is met with as a supplementary disorder.

Sometimes, especially in further advanced paralyses, there is painfulness of the nerves of the arms and legs on pressure and exceptionally also inflammatory swellings are observed on these limbs.

The muscles are, more frequently than the nerves, painful on pressure. Sensitiveness of the muscles of the calves is one of the commonest symptoms of beri-beri. Other muscles are also affected, and most extensively and severely in extreme paralysis. The tenderness of the abdomen on pressure, which is especially marked in the acute, pernicious form is, at least partly, attributable to hyperæsthesia of the abdominal muscles.

As to the *reflex activity* of beri-beri patients, the reflexes elicited from the *skin* are, according to my observations, normal and are only exceptionally lessened or increased. On the other hand, the *knee-jerks*, according to Jendrassik (Pekelharing and Winkler) are frequently absent, especially and almost without exception in all cases with pronounced paretic symptoms. This symptom is sometimes observed only a few days after the commencement of the illness and exceeds by months, or a year and even more, all other symptoms of the disease. Exaggerated knee-jerk has been observed by various authors (Pekelharing and Winkler, Däubler, Grimm, Norman, Miura, Carpenter) at the commencement of the disease, and when the course is acute ; Grimm regards this phenomenon as one of the most constant, and only exceptionally absent, symptoms of beri-beri. It is supposed to appear during the first three days of disease and to be of short duration, only existing about a week. According to my observations, the reflexes of the *cremaster* and abdominal muscles are rarely absent.

Serous exudations and exanthems are the most important of the *vaso-motor symptoms* (see below).

Glogner has recently called attention to the fact that the vaso-motor nerves participate more largely in the disease than has hitherto been supposed. By means of Winternitz's skin thermometer, he compared the temperature of the skin on various parts of the body (anterior surface of the leg, of the forearm and about 1 cm. above the navel) with the temperature of the axilla and anus of healthy persons and beri-beri patients, and in the latter he found that the temperature of the skin was on an average higher, even without there being any acceleration of the pulse, and this seems to prove the existence of vascular paralysis in the skin, or the subcutaneous muscles. The abnormal condition of the anal temperature, which was observed a few times, points to vaso-motor disturbances in the organs of the abdomen. By means of this hypothesis, he seeks to explain the vascular disturbances (condition of irritation or paralysis) in the circulation, which cause a greater fulness and tension of the vessels, and also a dilation of the pulmonary vessels ; it is also considered to explain the transient dyspnœa with strong cardiac activity, and without paresis of the respiratory muscles, that he has so frequently observed. He moreover considers that this explains the dilatation and hypertrophy of the right ventricle, the accentuation of the second pulmonary sound, the systolic murmurs at the pulmonary orifice, and the final stage

[1] *Die Grundzüge der Tropenhygiene*, 1895, p. 97.

of the acute pernicious form, at least in some of the cases. Several other symptoms
also, such as the diminution of the secretion of urine, the unequal distribution of blood
in the organs (paleness of one lung or kidney, with plethora of the other), the hyper-
trophy of the left ventricle, are attributed by Glogner to vaso-motor disturbances, and
he considers it justifiable to set up a separate *vaso-motor* form of beri-beri in addition
to a motor form and a mixed form.

All patients who are more or less paralysed, show a considerable
atrophy of the affected *muscles*, which, as a rule, increases in the limbs
from above downwards; it always attains its highest degree in the legs,
the calves often disappearing almost entirely. The atrophied muscles feel
relaxed and soft, almost like wadding. The paralysis and atrophy of the
muscles do not always run parallel, and the latter condition is frequently
hidden by dropsy.

At the commencement of the illness the muscles, according to Pekel-
haring and Winkler, are often extensively swollen and as hard as a board.
These authors identify such cases with Oudenhoven's polysarcous form
(see above, p. 203). According to Fiebig, this appearance is particularly
observable in the calves and in the posterior muscles of the thigh. Bälz,
like myself, has only seen this symptom on the muscles of the calves.
Such cases do not include those in which the muscular system is the
particular seat of serous exudations. The patients then appear as if
the entire body were much swollen, while pressure with the finger leaves
either no pit on the skin, or only here and there. I have never observed
this in acute cases with a fatal termination.

The *induration* of the *muscles of the calves*, already mentioned on p. 205,
must not be confused with the symptoms just described. This thicken-
ing is usually confined to the gastrocnemii, which may be felt as a hard
protuberance ending sharply below, but disappearing above, in the
popliteal space. This is a frequent symptom, according to my experience;
it sometimes only develops during convalescence, and may persist for
years after recovery from beri-beri.

Norman has recently directed attention to the *relaxation of the joints*
to be observed in the affected extremities, and which he is inclined to
attribute to trophic disturbances of the ligaments. In consequence, the
knees during the erect position assume a hyper-extended position which
would be impossible in the normal condition. The arch of the foot
becomes flattened, and flat-foot, which is sometimes very marked, ensues.
If the patient is made to assume the prone position, and the knees are
bent, the heel may be brought into contact with the buttocks. If the
leg is grasped and shaken, the foot swings about like a flail. This relaxa-
tion of the joints is observed not only in patients whose muscles are highly
atrophic, but also in those whose muscles are still well developed, and
whose gait is but little if at all disturbed.

The subcutaneous adipose tissue disappears, particularly from the
limbs, while the layer of fat on the trunk is but little affected, and in some
cases is even very well developed.

Atrophy of the skin is often exhibited in extreme paralysis, especially
on the limbs, and more particularly on the legs. The skin then appears
dry, coarse, lustreless, has lost its elasticity, and is covered here and there
with branny scales.

As to the remaining trophic disorders, decubitus is very rare and
principally occurs in complications with other serious illnesses, such as
typhoid fever, pulmonary phthisis, &c. In isolated cases the follow-
ing symptoms have been observed: Furuncles (Scheube), herpes zoster
(Laboulbène), erosions and vesicular eruptions often accompanied by

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loss of pigment (Lasnet), and non-articular inflammations of the joints (Scheube).

Cerebral symptoms (paralysis of cerebral nerves, see above, p. 204) play a subordinate part in beri-beri. Low spiritedness and a disinclination for mental exertion are a cause of complaint even in mild cases. More rarely there is heaviness of the head, headaches, rushes of blood to the head, singing in the ears, visual disturbances, disturbed sleep or, on the contrary, marked sleepiness at the commencement of the illness (Carpenter), and loss of memory. Consciousness is, as a rule, completely maintained, even in the most severe cases, to within a few moments before death.

In rare cases a diminution of the power of sight or complete blindness has been observed, particularly by Brazilian doctors. Komoto and Kono, according to Yamagiwa, confirmed central scotoma. In British North Borneo night blindness is, according to Carpenter. no unusual appearance. Œdema of the fundus oculi has been ophthalmoscopically found (Eldridge), retinal hæmorrhages, contraction and scanty contents of the retinal arteries, white striæ of various widths along the vessels, also whitish discolouration of the papillæ (Kessler), and optic neuritis (Mossé and Destarac).

Hardness of hearing was noted in a few cases by Brazilian doctors.

(2) *The Circulation.*—Next to the nervous system, the circulatory system suffers most in beri-beri. *Palpitation of the heart* is one of the most frequent symptoms of disease. At the commencement of the illness and in mild cases it only appears after violent movement of the body or after meals ; but during the further course of the disease it sets in when the patient is at rest, by predilection at evening or night-time, and may become the most troublesome of symptoms. It is frequently accompanied by *oppression* and *shortness of breath*. These symptoms are most intense in the acute pernicious form. Occasionally the patients complain less of palpitation over the heart than of palpitation in the region of the stomach.

Oppression sometimes sets in, not only as an accompanying symptom of palpitation of the heart, but independently, especially in the acute pernicious form, and is then apt to last longer and to be particularly severe at night.

Beri-beri patients complain of a feeling of fulness or pressure in the region of the stomach far more often than they do of oppression in the chest ; this, doubtless, has more to do with the heart than with the stomach.

Pains in the region of the heart occur in severe as well as in mild cases and are generally described as dull pains.

The *pulse*, as a rule, is more or less *accelerated*, sometimes even before any other symptoms of disease are exhibited. The pulse-frequency usually alternates between 80 and 100, and in severe cases, more particularly of the acute form, may attain to 120 or occasionally even to 140 beats per minute. The pulse is increased by the most trivial cause, such as movements, sitting up, &c.

Retardation of the pulse is far more rare, yet it may occur. I have observed it shortly before death, especially in severe acute cases. Elsberger, strange to say, found that the pulse as a rule was retarded.

Slight *irregularities of the pulse* are sometimes observed.

The pulse, as a rule, is *soft*, and the height of the sphygmographic curve varies according to the activity of the heart.

The *sphygmographic examination* shows that in mild and moderately severe cases the tension of the arteries is diminished, the elevations of the recoil are increased, the elevations of elasticity on the other hand are lessened or absent, and every transition is observed from a normal pulse to a sub-dicrotic, dicrotic, super-dicrotic, &c.

The *action of the heart* is frequently accentuated, and pulsation extends over an abnormally large area. Particularly before death the phenomenon of pulsation, extending far beyond the region of the heart and the upper part of the abdomen, is often observed ; the cardiac impulse exhibits a striking contrast to the small, weak pulse. Pulsation of the jugular vein is also observed in serious cases.

The *right ventricle* is frequently more or less dilated, *i.e.*, hypertrophied, and more rarely the left ventricle is simultaneously affected. In consequence of the high position of the paretic or paralysed diaphragm, the impulse of the heart in many serious cases is found at the fourth intercostal space outside the nipple line (Miura). Occasionally it will be found that a more or less marked hypertrophy of the left ventricle or of the entire heart is left as a heritage of beri-beri.

In the majority of cases systolic, and exceptionally also *diastolic*, *murmurs* are to be heard at one or other cardiac orifice, most frequently over the pulmonary and next at the mitral valve ; the diastolic murmurs are possibly functional only. Actual endocarditis is of great rarity in beri-beri.

Very frequently the second pulmonary sound is accentuated. More rarely there is a re-duplication of the same. Pekelharing and Winkler frequently found re-duplication of the first sound at the apex. In several cases described by Manson and Norman the rhythm of the cardiac sounds was reminiscent of the tick-tack of the clock, the first and second sounds being of equal length and the intervals between the two, and between the second and the following first sound, being almost equal.

In acute beri-beri Fiebig observed that there were sometimes systolic murmurs and *bruit de souffle* over the large arteries (carotids). Miura observed spontaneous arterial bruits over the femoral and brachial. Miura also mentions the occurrence of a certain diastolic arterial sound in the femoral which could be heard at a certain distance ; this was in severe cases.

The blood, examined during life, exhibits no particular characteristic. The number of red blood corpuscles is not lessened in mild cases ; in severe cases a decrease is observable during the course of the disease, and the hæmoglobin is still more diminished. The white blood corpuscles, according to my experience, are relatively increased in severe cases.

Däubler,[1] in three beri-beri convalescents, found that the particles of fat were increased in the blood (absorption of the fat of the diseased nerves).

On chemically examining the blood it is found that there is partly a decrease of the solid constituents, especially of the blood corpuscles and albumen, and an increase of the watery and mineral constituents (Schneider, Scharlée, Scheube), and partly a normal composition. This was the case in a patient suffering from an acute form only a few hours before death, and goes to prove that though *changes of the blood* occur frequently in beri-beri, yet they do not constitute *necessary accompaniments* of this disease.

Anæmia is a frequent but not a constant concomitant ; it is rarely absent, however, in serious cases.

Cyanosis is only observed in fatal cases ; it sets in only a short time before death.

The pigmentation of the skin and mucous membranes, of those nations amongst whom beri-beri is most frequent, prevents the cyanosis from appearing very distinctly, and accounts for the fact that not having the rosy complexion of Europeans, such people may appear to be anæmic without being so.

I have only observed *hæmorrhages* quite exceptionally, and in the form of bleeding from the gums and nose.

[1] *Arch. f. Schiffs- u Tropen-Hyg.*, i., 1897, p. 373.

In a few cases I observed *inflammatory enlargements of lymphatic glands*, especially of the groin glands or groin and femoral glands, which sometimes suppurated; they usually precede the other symptoms of disease or set in simultaneously with them without a local cause for their appearance being discoverable. This observation was made by Fiebig, and according to Königer, a few cases of glandular enlargements occurred also during the epidemic of beri-beri that raged in Manila in 1882-3, so that at first the disease was taken for a species of bubonic plague.

(3) *Respiratory Organs.*—*Shortness of breath* frequently accompanies the palpitation of the heart, and attains its highest degree in the final stage of the acute pernicious form. The breath, like the pulse, is more or less accelerated as a rule, even in cases in which there is no subjective dyspnœa and no palpitation of the heart.

Colds in the head, inflammation of the throat, mild laryngeal, tracheal and bronchial catarrhs occasionally occur in beri-beri; these sometimes introduce the disease and sometimes set in during its course. I have never observed inflammation of the lungs. Lasnet's patients suffered from an almost continuous tormenting cough.

Œdema of the lungs is generally the finale in the acute pernicious form.

(4) *Digestive Organs.*—Disorders of the stomach are frequent, but by no means regular, symptoms of beri-beri. There are frequently complaints of a sensation of fulness or pressure in the region of the stomach, this is sometimes only felt after meals, and is sometimes always present. There is often also pains in the stomach that generally set in after food, and heartburn and sour eructations are not uncommon symptoms. In serious cases, mostly of the acute pernicious form, the patients refuse almost all nourishment, but are, as a rule, tormented by burning thirst. There is occasionally an abnormal sensation of hunger. The tongue is more or less coated, even in those cases in which there are no disorders of the stomach.

Retching and *vomiting* are but rarely concomitants of beri-beri and mostly occur in the acute pernicious form accompanying the serious disturbances of the circulation and respiration that precede the fatal issue.

The *stool* is frequently *constipated*. *Diarrhœa* is much less common, but sometimes it precedes the other beri-beri symptoms. I occasionally observed involuntary evacuations of fæces during the last days of life.

Lasnet observed the vomiting of *bloody mucus* in the acute pernicious form. I exceptionally observed bloody stools in the acute pernicious form, and I likewise saw violent *tenesmus* simultaneously with other transient spinal cord phenomena, such as retention of urine and decubitus.

The *liver* as a rule exhibits no symptoms, though in the acute form enlargement of that organ is sometimes observed. Jaundice does not occur. Enlargement of the spleen is not demonstrable in uncomplicated forms.

(5) *Urinary and Sexual Organs.*—The *quantity of urine* is, as a rule, diminished, and most considerably so in the acute pernicious form, in which it sometimes falls to 40 or even 30 ccm. in twenty-four hours; entire cessation of the secretion of urine may even take place. Every improvement of the condition is apt to be accompanied by an increase of the secretion of urine. This is particularly the case in the dropsical form, in which, when the serous exudations are re-absorbed, the daily quantity of urine not rarely increases to 2 to 4 litres, or more.

The *specific* gravity of the urine generally stands in direct ratio to its quantity, and is, according to my observations, *relatively diminished*.

The *colour of the urine* varies according to the degree to which the urine is diminished.

According to my investigations the secretion of *urea, uric* acid, and *phosphoric* acid is diminished, the relative estimation of the latter, however, is mostly increased (Zülzer). This indicates an increase in the destruction of nerve-tissue, whereas in other respects the albuminoid substance is diminished in consequence of the lessened supply of nutriment. The excretion of salts runs parallel with the quantity of urine, and is sometimes considerably increased at the period when the dropsical exudations are absorbed, with considerable increase in the quantity of urine.

Sugar has never been demonstrated, but Bälz found an abnormally copious quantity of indican.

Albuminuria is but seldom observed, and only in the acute pernicious form during the last period of the disease.

I observed one case in which several attacks of beri-beri were accompanied by slight renal inflammation.

It is very rarely that difficulty in emptying the bladder, cramp, or paralysis of the bladder are observed.

Sexual impulses and generative powers decrease and may be completely lost. Thurm mentions the occurrence of painful erections and Sodré Pereira of frequent involuntary escape of semen at the commencement of the disease.

In women *menstruation* is suspended during the disease and returns on recovery.

(6) *Skin and Serous Membranes.*—The colour and condition of the skin has already been considered.

The *secretion of sweat* is frequently diminished on the affected limbs, especially in severe cases; sometimes it is increased.

In convalescence from severe attacks the hair of the head sometimes falls out.

Exceptionally, *exanthems* such as petechiæ, erythema multiforme, herpes labialis, &c., are observed in beri-beri. I have, however, only seen spotty or diffuse redness in isolated cases; whereas according to Miura this is of frequent occurrence and is especially observable on the legs when standing up, or on the arms when they hang down.

Œdema is one of the most constant symptoms of the disease and it may appear in all the forms. The legs are its seat by predilection and it is apt to make its first appearance over the inner surface of the tibia or on the dorsum of the foot, but it frequently varies in intensity. The highest degree of œdema is observable in the dropsical or dropsical-atrophic form, in which the dropsy spreads more or less to the other parts of the body, the face, the arms, the trunk, the genitals, and in which also collections of fluid develop in the serous cavities. According to my observations dropsy of the pericardium occurs most frequently, and more rarely hydrothorax and ascitis. Occasionally the serous cavities, or one of them, is almost the exclusive seat of the exudations, while the sub-cutaneous cellular tissue is almost free from œdema. In the acute pernicious form dropsy of the cavities is also observed, but it does not obtain to the same extent as in the dropsical form. Däubler and Norman occasionally saw slight effusions in the joints, more especially the knee joints. Spencer and Grimm, in rare cases, observed œdema of the *mucous membranes* (conjunctivæ, oral cavity, pharyngeal cavity, larynx).

Circumscribed œdemas are a peculiar phenomenon; these mostly make their appearance on the upper part of the body, on the face, neck and trunk. In my experience these hypostatic swellings are attributable to the diminished action of the heart; they constitute therefore an unfavourable sign.

Inflammations of the serous membranes are very rarely met with in beri-beri.

(7) *General Condition.*—In the majority of patients there is a pronounced *feeling of general indisposition* at the commencement of the illness, even in the mildest forms.

The *expression of the face* in most patients exhibits nothing remarkable. In the acute cases with a fatal termination, the utmost anguish and restlessness is apparent on the features during the final stage. In patients suffering from the atrophic form the severity of the muscular pains they endure may be read in the countenance.

The *condition of nutrition* has already been considered (see above, p. 212).

Fever is not a constant symptom of beri-beri. Many cases run their course from beginning to end without fever; in other cases a rise of temperature lasting one or several days is observed, partly at the beginning of the illness, partly during its course. When the fever only lasts one day it is not rarely accompanied by catarrhal symptoms; when lasting longer it is frequently induced by a change for the worst, or the development of complications. According to my experience the fever is never very high, 39° being rarely exceeded. In regard to fever, moreover, local and periodical conditions influence it.

According to Grimm *rise of temperature* (from 1·10° above normal to 39°, or even 40°) is one of the most *constant* symptoms of beri-beri, though it does not persist for long, often only one or two days, and at the utmost five to seven days. Grimm ascribes an increase of temperature setting in during the course of the disease to indicate a new infection (see above p. 203).

Recovery is the most frequent termination to beri-beri. In many cases, however, the cure is not a complete one; disorders remain for a long time, some of them for the entire period of life, occasionally debarring the patient from being considered able-bodied again.

The *sequelæ of the disease,* according to my observations, principally affect the nervous system and the circulation. Of the sequelæ the following are worthy of mention : Languor, heaviness and weakness of the lower extremities, particularly the legs, occasionally one only being affected; contraction and induration of the muscles of the calves, and disorders of mobility of the upper extremities; diminution of sensation on different spots of the skin, more especially on the legs ; also a feeling of cold, of numbness, pains, painfulness of certain spinous processes on pressure, absence of knee-jerk, palpitation of the heart, acceleration of the frequency of the pulse, hypertrophy of the left ventricle, weakness of the heart, accompanied mostly by dilatation of the right ventricle, and of œdema setting in periodically. Sometimes, also, weakness of the memory, melancholia, and enlargement of the liver, have been observed as sequelæ.

Miura entirely eschews the occurrence of sequelæ. He says: "When kakke terminates in recovery, it is always a complete one."

I may take the opportunity of here mentioning a fact mentioned by Zwaardemaker and Kraft and which I can corroborate by a case observed in Germany, namely, that in European beri-beri patients who have returned home convalescence is generally very slow, and recovery may take months or even years to accomplish.

The *percentage of mortality* from beri-beri varies according to time and place. It is not only different in the several beri-beri countries, but the malignancy of the disease varies in different parts of the same country, and even a different form of the ailment may be exhibited in successive years in the same places of the same country. As a general rule it may

be taken that the mortality formerly was greater than it has been in recent times. Of the three principal centres of beri-beri the Dutch Indies, Japan and Brazil, the disease exhibits the mildest character in Japan, and the most malignant character in Brazil. In Japan I observed an average mortality of 3·7 per cent., whereas Bälz only computes it to be $2\frac{1}{2}$ per cent. at the highest. According to van der Burg, the mortality in the Dutch Indian army varied, during the period from 1884 to 1894, between 2·83 per cent. (1891), and 6·12 per cent. (1885), giving an average of 4·43 per cent. In Brazil, from whence we have no recent reports, the mortality, according to Da Silva Lima, fluctuated between 50·8 per cent. and 74·5 per cent.

Death in *acute cases* mostly ensues in consequence of *paralysis of the heart*, which may set in suddenly, or in consequence of *paralysis of the diaphragm*, or in consequence of the simultaneous effect of both causes ; it is caused more rarely through *embolism of the pulmonary arteries*. According to Da Silva Lima, *uræmic conditions* may likewise be the cause of death.

In chronic cases, especially those that are complicated with other severe diseases, such as typhoid, dysentery, pulmonary phthisis, &c., the patients succumb to *general* exhaustion.

PATHOLOGICAL ANATOMY.

Beri-beri cadavers mostly only exhibit a slight and short rigor mortis. *Post-mortem* lividity appears early.

The face, when the course is an acute one, is cyanotic and swollen, the eyes are staring, there are extravasations of blood into the connective tissues, there is froth at the mouth, and the veins of the neck are enlarged. In rare cases the entire body is cyanotic, and covered with extravasations under the skin.

In *chronic cases* the cadaver has a pallid appearance. If dropsy had been present, the body appears more or less swollen ; in atrophic cases, on the other hand, it is very emaciated.

In addition to, or even without, œdema there is frequently dropsy of the cavities, pericardial dropsy being the most frequent. The effusion into the pericardium may amount to 2 c. (van Leent). Often, however, the quantity is so insignificant, exclusive of the cases in which no fluid at all is in the pericardium, that it could only have played a subordinate part in causing death.

Punctiform hæmorrhages under the visceral layer of the *serous pericardium* and of the *pleura*, are frequently met with.

The *heart* is usually enlarged, the right ventricle especially is almost always dilated, and it may also frequently be hypertrophied ; more rarely the wall of the left ventricle is thickened.

In 125 *post-mortem* examinations of beri-beri cases made by Ellis the mean weight of the heart was 13·37 English ozs., while in 204 other cases the average weight was not 9 ozs.

The *myocardium* is more or less fatty. I have never failed to observe this condition under the microscope in every case. Yamagiwa, in almost 50 per cent. of the cases, found the myocardium more or less opaque, or in a state of marked fatty degeneration.

Various observers (Scheube, Bälz, Pekelharing and Winkler, Fiebig) found small *myocarditic foci*, similar to those occurring in diphtheria and other infectious diseases. In several cases I also observed infiltrations

of young cells into the subpericardial cellular tissue, and exceptionally I saw small hæmorrhages into the myocardium, and beneath the endocardium.

In regard to this condition of the heart in beri-beri, the results attained by A. Hofmann (Eichhorst[1]) *after bilateral excision of the vagus* in rabbits in which tracheotomy had been performed are of great interest. The animals died after from twenty to fifty-eight hours, and the following condition prevailed : Fatty degeneration of the cardiac muscle, small hæmorrhages between the muscular fibres, and cellular agglomerations between these, particularly beneath the endocardium and pericardium ; the lungs meanwhile were intact, or exhibited only slight changes.

The *blood* in the cadaver is dark red, and is remarkably fluid ; it is mostly found uncoagulated, and on exposure to the air it clots slowly.

This want of coagulation is, according to Miura, probably attributable to the quantity of carbonic acid it contains.

Very rarely ante-mortem *coagulations* from embolisms are found in the right ventricle, in the pulmonary arteries, &c.

In cases that have died from the acute form, the quantity of blood that escapes, even when small veins are incised, is remarkable.

Lodewijks and Weiss regularly found *endarteritis* of the aorta and larger arteries of the upper part of the body, and regard these as responsible for the signs and symptoms present in beri-beri. Their observations have, however, not been confirmed by other observers.

The *lungs*, especially the lower lobes, are, as a rule, hyperæmic and œdematous. There is frequently more or less extensive emphysema, which particularly affects the anterior edges and the apices of the lungs.

The *intestinal canal* in most cases exhibits venous hyperæmia in varying extent and severity, often also small hæmorrhages in the mucous membrane and œdematous swelling of the latter. The *stomach*, as a rule, exhibits the appearance of hæmorrhagic erosions.

Intestinal parasites, especially anchylostomum duodenale and trichocephalus dispar, are frequently found, but are not ætiological factors in beri-beri, as has been asserted (Erni, Kynsey).

The *liver* is often enlarged and generally congested, in consequence of the universal venous engorgement ; occasionally also well-marked nutmeg liver is met with. Microscopically, as a rule, granular opaqueness and fatty changes of the cellular elements are present. I have several times found small granular agglomerations in the connective tissue between the lobes, as well as within the lobes.

In regard to the *spleen*, accounts differ. Some observers found it normal, sometimes even atrophic, and others found it enlarged. My observations are in accordance with Fiebig's and others, and show that enlargement of the spleen, even though insignificant, is the rule in beri-beri.

Ellis, in 125 cases of beri-beri, found that the spleen on an average weighed 9·27 ounces, in 204 other cases the average weight was 6·28 ounces.

The *kidneys* usually show hyperæmia and cloudy swelling, with granular changes in their cellular elements. I several times found agglomerations of young cells, usually beneath the capsule ; and I likewise observed hæmorrhage into the pelvis of the kidneys a few times Miura several times observed glomerular nephritis.

The *nervous system* exhibits the most important morbid changes, and

[1] *Virch. Arch.*, cl., 1897, No. 1, p. 161.

it is the peripheral nerves which in beri-beri form the principal seat of disease.

The peripheral nerves, as seen with the naked eye, seldom exhibit any abnormality; though in a few injection of, and hæmorrhages into, the sheath as well as into the nerves themselves may be observed.

Microscopically the nerves, as was first pointed out by Bälz and myself, exhibit a more or less marked degenerative inflammation; disintegration of the medullary sheath and also of the axis cylinder, increase of the nuclei of the endoneurium and beneath the perineurium, particularly in the vicinity of vessels, being noted in chronic cases; finally, increase of the connective tissue (see figs. 21-24, table II.).

Pekelharing and Winkler, and Yamagiwa only found simple degeneration of the nerves without increase of nuclei of the vessels.

A portion of the fibres of all the spinal nerves are probably attacked by these changes; they are, however, mostly found in the nerves of the limbs.

The muscular branches are always affected to the greatest extent, whereas the nerve trunks exhibit few changes, or may even appear normal. Even purely sensory cutaneous nerves are attacked by the disease. The degree of degenerative inflammation, as a rule, corresponds with the symptoms of paralysis exhibited during life. The highest degree is therefore observed in chronic cases; while in those of the acute form, associated as a rule with a minor degree of paralysis existing during life, only the initial stage of degenerative inflammation is to be found and even this may be absent (Fiebig, Ellis). Often only isolated patches appear diseased, while those in their vicinity appear to be normal. This is undoubtedly connected with the different origins and the different activity of the portions attacked (Bälz).

In acute cases the disease extends to the *vagus and its branches*, the cardiac and pulmonary nerves, the laryngeal nerves, and occasionally also to the phrenics. v. Tunzelmann and Ellis found the nerves to the arteries diseased, and Ellis also found the splanchnics, the solar and renal plexuses and the mesenteric branches affected. Bälz also observed degeneration of the renal nerves in one acute case in which the secretion of urine had almost completely ceased.

Degenerative inflammation of the *muscles* goes hand in hand with that of the nerves. According to the degree of the disease fewer or more muscular fibres are found to be in a state of fatty degeneration, their transverse striation indistinct or entirely obliterated, and the nuclei of muscle fibres increased. Besides the fatty degeneration, colloid and other similar degeneration occurs, in which the muscular fibres become attenuated, their transverse striation is gradually lost, they become homogeneous and their fibrils split. In transverse sections in recent cases (see fig. 25, table II.) one finds, besides muscular fibres of normal and decreased size, large swollen muscular fibres and agglomerations of nuclei in the connective tissue between the bundles of muscles, and also between the muscular fibres; in further advanced cases (fig. 26, table II.) the muscular fibres are found to be considerably attenuated, the connective tissue increased and nucleated, and the walls of the vessels thickened. Muscles changed in this manner are perceptible to the naked eye on account of their pallor and yellowish colour. Pekelharing and Winkler also observed hæmorrhages into and between the muscles.

The *muscles of the calves* are always most diseased.

As to the spinal cord there are not uncommonly macroscopical signs of

venous hyperæmia of the spinal meninges and serous effusions into the
peri-dural and subarachnoid spaces. Microscopically the condition as a
rule is quite normal and the changes found in a few cases (proliferation of
the cells of the central canal with infiltration of the ganglion cells in the
vicinity, atrophy of the ganglion cells of the anterior cornu) are quite
unimportant, or of a secondary nature.

Pekelharing and Winkler, in one case observed double-sided ascending degeneration
in the *posterior column*, with atrophy of the medullated nerve filaments in the *anterior
roots*. Miura (according to Yamagiwa) found simple atrophy of the *posterior column* in
three out of eighteen cases histologically examined by him. In a few cases Pekelharing
and Winkler and I found the spinal ganglia diseased, showing nucleated infiltration
of the connective tissue and of the nerve roots, with an increase of the finer fibres,
especially in the periphery.

The *softened areas* so frequently met with in the spinal cord, and also the equally
frequent amyloid bodies, are *post-mortem* changes.

The medulla oblongata was found normal by Pekelharing and Winkler.

Lately Küstermann had a case (Chinese) in Hamburg for *post-mortem* examination.
Besides advanced degeneration of the vagus, there was acute degeneration of its
ganglion at the base of the fourth ventricle. The tissues round the distended vessels
were œdematous and permeated by numerous capillary hæmorrhages, the ganglion cells
were shrunken and lessened in number. The remaining nerve nuclei of the medulla
oblongata were normal.

The usual conditions in the *brain* are, according to my observations,
venous hyperæmia of the cerebral meninges, œdema of the connective
tissues and hyperæmia of the brain substance. Occasionally the fluid of
the cerebral ventricles is increased, and œdema and anæmia of the brain
substance also occur. Miura found nothing abnormal microscopically.

Pekelharing and Winkler could discover no changes in the *bone
marrow*.

The various aspects, signs and symptoms of beri-beri are readily
explained away on the basis of the anatomical changes productive of
multiple peripheral neuritis. Motor and sensory paralysis, at times
amounting, especially in the lower limbs, to paraplegia, advances coinci-
dently with atrophy of paralysed muscles.

The heart symptoms are attributable to the affection of the cardiac
vagi, which also contain the trophic fibres for the heart. Their disease,
therefore, induces a disturbance of nutrition of the heart which is
exhibited anatomically by fatty degeneration and leads to weakness and
finally to paralysis of the myocardium. Besides these causes the inflam-
matory changes occurring in the myocardium, as well as the serous
exudations into the pericardium, exercise an influence on the action of the
heart.

von Tunzelmann attributes the sinking of blood pressure, which in most cases
precedes death, not to paralysis of the heart, but to paralysis of the vaso-motor fibres.

The *serous exudations* are caused first and foremost by the disease of
the vaso-motor or analogous fibres. In more advanced forms of beri-
beri they are further caused by the weakened action of the heart and
the venous engorgement produced thereby, and by the altered condition
of the blood, which consists in an increase in the proportion of water
and a decrease in the proportion of albumen.

The *diminution of the secretion of urine* is explained partly by the
disease of the nerves of the kidneys, partly by the enfeebled action of the
heart.

The *spinal cord never becomes primarily diseased* in beri-beri, but
exceptionally the disease may reach it along the nerve roots. That this

happened in one patient that came under my observation would appear to be the case from the fact that the sphincters were attacked and bed sores set in.

The different forms of the disease are due to the unequal degree in which the several systems suffer. In the atrophic form the sensory and motor nerve fibres with the muscles are principally attacked; in the dropsical form the vaso-motor nerves are affected; in the acute pernicious form the cardiac vagi; while in the rudimentary form all these various systems are frequently slightly attacked.

DIAGNOSIS.

The diagnosis of beri-beri offers no difficulties in most cases. The following symptoms are important for the recognition of cases just commencing. Diminution of sensation on circumscribed spots on the legs or feet; œdema on the inner surface of the legs; sensitiveness of the calves of the legs to pressure; absence or exaggeration of knee-jerk; palpitation of the heart; acceleration and slight excitability of the pulse, especially on movement or on assuming an upright position.

Cases, however, frequently occur in which the diagnosis cannot be established and further observation of the patient is necessary. This is particularly the case when the disease is preceded for some time by indefinite complaints of what might appertain equally to beri-beri or any other disease, or when serous effusions into the subcutaneous tissues and into the serous cavities, or into the latter alone, precede the characteristic symptoms. In exhausted, bedridden persons, such as typhoid patients, consumptives, &c., it is easy to overlook beri-beri setting in, when examinations are not specially undertaken with a view to confirming its presence.

As to confusing other diseases with beri-beri, such a mistake is hardly possible as regards heart or kidney diseases when a careful examination has been made. As to *spinal meningitis, tabes dorsalis, progressive muscular atrophy, anchylostomiasis, trichinæ*, &c., though beri-beri may bear some likeness to these it is easily to be distinguished from any one of them.

PROGNOSIS.

Notwithstanding the favourable termination of beri-beri in most cases, it is impossible to prophecy the issue with absolute certainty in individual cases; one cannot be positive in any case that sooner or later threatening symptoms of heart affection may not set in.

The *disturbances of the circulation* are therefore of great importance in determining the prognosis. Should a patient early in the disease exhibit rapidly increasing cardiac phenomena, one must be prepared to expect an unfavourable termination. On the other hand, in patients considerably paralysed a favourable issue may be anticipated if the cardiac phenomena are absent, or if they only play a subordinate part. Under such circumstances even severe cases of the dropsical form afford a good prognosis.

Vomiting and circumscribed œdema may be regarded as unfavourable symptoms; increase of the urinary secretion and the return of a healthy appetite are favourable signs. In Brazil also, as Féris asserts, permanent

erections and an immoderate desire for sexual intercourse, especially in young men, is regarded as a good sign.

Certain complications exercise a great influence on the prognosis; complications with secondary syphilis, alcoholism, addiction to opium, pleurisy, diseases of the respiratory organs (bronchitis, emphysema, pneumonia) in which the respiratory muscles are paretic and expectoration therefore impossible (Grimm), icterus from whatever cause, defective action of the kidneys, and, last but not least, dysentery, are all considered to be unfavourable signs.

PROPHYLAXIS.

The measures required for the prophylaxis of beri-beri are :—Improved means of draining the soil, procuring pure drinking water, care in having cleanly, roomy, and well ventilated dwellings. In districts where the disease rages severely endemically it is necessary that houses should be separated from the ground by an impervious layer (cement or asphalt), so that the ground air and damp cannot penetrate.

Buildings to which the virus of disease clings, such as barracks, jails, hospitals, &c., must be submitted to thorough cleaning and disinfection, regularly repeated. The inmates of such buildings must be examined periodically, and those who prove to be affected with even the slightest symptoms must leave the premises. The linen, clothes and other possessions of the patients must be disinfected, as the virus of the disease may be carried by inanimate objects.

The crews of ships should always be examined before a voyage and sick men should be left behind. Should cases of the disease occur during the voyage, the patients should be placed in well ventilated cabins or brought on deck. Ships on which cases of beri-beri have broken out, or that have had patients on board, must be disinfected.

TREATMENT.

No specific remedy for beri-beri has been discovered.

The favourable influence exercised by change of climate and *removal of the patient from beri-beri regions* to healthy high-lying places has long been known. The result is mostly immediate and surprisingly favourable. Sometimes, also, removal from the house where the disease took place to even a neighbouring house has a favourable effect (Fiebig, Kessler). Removal of the patient to any distance, however, can only be undertaken in mild cases or in cases of medium severity; in patients suffering from weakness of the heart or general dropsy such a proceeding would do more harm than good. *Sea voyages* are as advantageous as change of climate. Weintraub considers it necessary that Europeans should *return to Europe* and stay there for at least two years, as his experience in the Dutch Indies has proved that beri-beri convalescents of European descent are soon again attacked if they return to the Indies after only a short stay at home.

Some doctors are greatly in favour of *aperients*, especially at the commencement of the disease, such as sulphate of soda, Carlsbad salts, sulphate of magnesia in large doses being preferred. I was unable to obtain any beneficial results from these drugs. The fact, also, should not

be lost sight of that their prolonged use tends to weaken the body. Good results were attained by me from the use of small doses of Carlsbad salts for the relief of the digestive disorders and constipation in beri-beri. In acute cases Anderson advises strong intestinal derivatives, such as one or two drops of croton oil with 0·3 calomel.

In fresh cases some doctors prescribe *salicylic acid* or *salicylate of soda*. Bälz made use of salicylic acid (1·0, four to five times daily) alternately with pilocarpin (0·02), and with this treatment he observed that all the symptoms of disease were removed, often in a few days. I have not seen any favourable results ensue from these drugs and I am not aware if the salicylic acid has an effect analogous to those remedies of more recent date, antipyrin, antifebrin, &c.

Digitalis is an indispensable drug in beri-beri and has rendered me good service not only for palpitation of the heart, but for dropsy also. As a remedy for dropsy I frequently administered digitalis in conjunction with other diuretics, such as acetate of potassium, squills, and always at the same time used *strong stimulants*, such as large doses of camphor or subcutaneous injections of ether. Under this treatment I have seen even the most intense dropsy disappear, and I have never been obliged to have recourse to tapping. In patients with the acute form who, on admission to the hospital, are found to be suffering from pronounced cardiac insufficiency, this, like every other form of treatment, proved without effect. On the other hand I am convinced that in several cases in which a rapid increase of the cardiac symptoms led to the fear of an unfavourable termination, the danger was averted by this treatment.

In the place of digitalis, the following are also recommended, digitalin, tinct. strophanthi, caffeine and its adjuncts, diuretin. Extract of belladonna sometimes also proved effective in palpitation of the heart.

In several cases of acute beri-beri threatening paralysis of the heart, Bälz found cocaine, which is an excellent heart tonic, very useful. Simon (according to Manson) in such cases recommends five to ten drops of a 1 per cent. solution of nitro-glycerine every quarter or half-hour.

In acute cases with intense cardiac insufficiency, *phlebotomy* is the last resource. To the best of my knowledge this treatment was· first used by Marshall, and it has lately been warmly recommended, especially by Anderson and Bälz. According to Bälz it suffices to draw from 300 to 400 g. of blood. The favourable effect is due to the relief of the heart. Personally, my experience is that phlebotomy only affords evanescent relief, and not permanent results. I, however, only resolved to carry out this measure (as advised by Bälz) when I had convinced myself that there was no other resource. Recently Miura has given the advice not to put off the venesection too long, but to undertake it before the cardiac action is sunk too low and whilst the impulse of the heart's apex can be still felt. Miura abstracted the blood by means of cupping glasses, generally taking 100 to 250 ccm. in two or three sittings, or he applied 60 to 80 small Japanese *leeches* to the chest of the patient while applying the faradaic or galvanic current to the phrenics. Miura got excellent results by this treatment.

Morphia injections have good results in relieving the *oppression* and *dyspnœa* which torture the patients in the acute form of the disease; they also had a good effect in allaying *vomiting*.

In severe *hyperæsthesia* bromide of potassium, with inunctions of oil of chloroform, and, if necessary, injections of morphia are indicated.

When the course of the disease is more chronic, and more particularly during convalescence, arsenic (Fowler's solution) with iron, decoctions of quinine and other tonics should be administered.

I have seen decidedly favourable results ensue in the atrophic form by *electrical treatment* of the paralyses.

The galvanic current is applied (cathode peripherally to the nerves, anode centrally); and when the atrophy of the muscles is great, in addition to the galvanising of the nerves, faradisation of the muscles (stroking the muscles with large sponge electrodes or massage cylinders). It is, however, advisable only to commence the electrical treatment when the disease has come to a standstill (reached its maximum).

In *paralysis* of the *diaphragm*, Miura recommends faradisation of the phrenics with sponge electrodes, of which one is placed over the pit of the stomach and the other behind the sterno-cleido-mastoid muscle at the clavicle, or both may be placed on the neck ; the treatment to last five to ten minutes.

I found no effect worth mentioning accrue from injections of *strychnine*, which are highly recommended by some doctors.

Suitable *methodical exercises* and *massage* of the paralysed muscles should be administered with the electrical treatment, along with *warm baths* and other mild *hydropathic processes*. According to Bälz, however, hot baths and sea baths are positively injurious.

Finally, two important remedies must not be forgotten, rest and diet. In every severe case *rest* of the diseased part, especially rest in bed, is the first and most important measure indicated. Bälz, however, does not advise the entire avoidance of walking at the commencement of the illness, but thinks the patients should continue to make moderate movements (to induce circulation in the diseased members), while all severe exertions should be entirely avoided.

Easily digestible but nourishing food should be chosen as the *diet* of beri-beri patients. Milk is particularly suitable on account of its diuretic properties. Tea is recommended as a drink for the same reason. In convalescents, with large appetites, Bälz found a form of Weir-Mitchell treatment was effective.

Japanese doctors are much given to ordering a *species of bean* (phaseolus radiatus, Japanese : adzuki), which possesses diuretic properties, as food.

LITERATURE.

A complete compendium of literature is contained in my monograph on beri-beri. In referring the reader to this I beg to state that in the present work I only make mention of the literature published, according to my knowledge, since then (1894), as also of the works used by me.

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IX.

CLIMATIC BUBOES.

DURING recent years a number of publications have appeared on a disease which, provisionally, has not unsuitably been termed "climatic buboes." In 1896 Ruge reported 38 cases of inguinal glandular enlargement which had been observed in the blockade squadron on the Zanzibar coast during 1888 and 1889. In these cases none of the usual causes could be traced (sexual diseases, injuries), and Ruge regarded them, therefore, as climatic. The disease presented many variations. Sometimes the illness began with fever, or fever only set in when the bubo increased in size, or when suppuration occurred; the fever exhibited nothing typical, and sometimes the affection ran an entirely afebrile course. The enlargement of the inguinal glands was mostly confined to one side; occasionally both sides were affected simultaneously, or one after the other. The glandular swelling generally developed quickly, within a few days, and sometimes attained the size of a goose egg. It consisted sometimes of a group of glands, sometimes of separate contiguous glands. In 60·5 per cent. of the cases the swellings, notwithstanding their great size, became absorbed, and in the remaining 39·5 per cent. the buboes had to be operated on. Sometimes they were incised, when distinct fluctuation set in; sometimes, when the patient had suffered much or become enfeebled by the long duration of the illness, the diseased glands were excised. The duration of the illness varied between a few days and a few months. No case had a fatal termination. Relapses occurred sometimes on the side previously affected, sometimes on the other side.

Two English publications are quite independent of Ruge's report. Godding relates the occurrence of the "non-venereal bubo" in the English navy, and is of opinion that climatic conditions play a large part in its etiology. The signs of the disease consists in enlargement of the inguinal glands of one or, more rarely, both sides; indisposition; fever, which, according to the chart accompanying the article, is an irregular remittent; and anæmia. As a rule the swelling becomes absorbed; suppuration is rare, but is frequently erroneously supposed to be present on account of the bubo becoming soft and fluctuating. The disease lasts a few weeks or months. In some cases a slight strain seems to have furnished the exciting cause, in others, a superficial abrasion on the penis or toes; but more frequently no cause whatever can be indicated. Age seems to exercise no influence. The affection is most frequently observed in the East Indies and China station of the English navy. In the years 1888-1894, and with a mean strength of 56,180 men, 733 cases on an average were observed yearly in the English navy. Most cases occurred

in the East Indies (31 cases to 1,000 men), China (25 per 1,000), and the West Indies (22 per 1,000) ; the fewest in the Mediterranean Sea (8 per 1,000), Australia (9 per 1,000), and on the west coast of Africa (13 per 1,000). England and the English Channel furnished 10½ per 1,000 cases. In a later publication Godding says that the disease is most severe on the East African coast, but he quotes no figures.

Skinner, in the presidency of Bengal, observed numerous cases of inguinal buboes of unknown origin. Of 49 cases that occurred in a regiment and one battery, 28 came under observation in Calcutta, 13 in Hong Kong, 4 in England, 2 in Allahabad, and 2 in Malta. Generally the appearance of the buboes was preceded by fever, which was usually remittent. The patients were frequently cachectic, and had previously suffered from malaria. Sometimes the buboes appeared while the patients were under treatment for climatic fever or dysentery.

Schön Halfhide, moreover, mentions that idiopathic suppurations of lymphatic glands occur in Coronie (Surinam) and that they are often complicated with peritonitic symptoms.

There is another statement by Nagel, who, in German East Africa, saw a number of cases of buboes in which all other etiological factors were excluded, and which therefore could only be ascribed to climatic influences ; officials and planters who had been in East Africa over a year were mostly affected, and a certain proportion of the cases had suffered, or were still suffering (2 cases), from malaria. In no case did the fever exceed 39°, and in only two patients did suppuration set in, when the glands were incised.

The swellings mostly developed quickly and were more or less painful. In one case, for a week previous to the swelling becoming perceptible there was severe pain, especially on pressure in the inguinal region. Recovery was comparatively quick, and the fever abated after the local affection had healed.

In Japan (Kioto) I myself observed sixteen similar cases. The glandular enlargement affected the inguinal glands with the exception of one case, in which the femoral glands were affected ; the enlargement was mostly on one side, only in one case was it bilateral. In four cases there was suppuration, the abscess either opening spontaneously or it was incised. The disease sometimes had an afebrile course, and was sometimes, especially at the beginning, accompanied by fever, which in one case preceded the appearance of the glandular enlargement by ten days, and was of an intermittent type. In several cases the illness dragged on for several months. In other respects it exhibited nothing characteristic.

Most of my cases were in young men of from 17 to 29 years of age, who had the most diverse occupations, and only two older persons, a man aged 46, and a woman aged 49, were amongst them. The majority of cases came under observation in the spring and autumn. Most of Ruge's cases likewise occurred from September to November, and from March to May ; the other authors furnish no information as to the season in which the disease appeared.

There is no doubt that all these observations relate to the same ailment. Even though the clinical features of the disease drawn by different authors are not similar in all points, yet they show no greater deviation than every separately observed group of cases do.

All observers deny the connection of the disease with *malaria*. Ruge excludes paludism as the exciting cause of his cases because he has repeatedly been able to observe that the fever, which previously had defied quinine, disappeared as soon as the diseased glands had been

removed, and amongst the numerous cases of malaria that were observed simultaneously in the blockade squadron not a single case was complicated with inflammation of the inguinal glands. Godding asserts that splenic enlargement has only been mentioned in one case ; Nagel found that quinine had not the slightest effect upon the course of the disease ; Skinner in several cases vainly sought for the malaria parasite, nor could I find any connection with malaria.

Probably several other observations belong to the same illness, although these are summed up by the various authors who communicate them as a form of malaria.

Martin observed that in Deli, on the north-eastern coast of Sumatra, patients who had previously suffered from malaria and exhibited initial or more advanced cachexia, often suffered from remittent fever accompanied by inflammatory swelling of the inguinal, or more rarely of the femoral, glands. These glandular enlargements were not very painful, but often attained enormous dimensions. If treated suitably by change of climate, or as by Priessnitz with graduated compresses, quinine, arsenic and iron, &c., the fever and swelling quickly abated ; when suppuration occurs the pus burrows and leaves ugly fistulous tracts difficult to heal, while the cachexia rapidly advances.

Martin considers these cases are of a malarial nature from the fact that they occur in malaria convalescents or malarial cachectics and recover under suitable treatment. If, however, one takes into consideration the fact that Martin's field of observation is a notorious malarious district—80 per cent. to 90 per cent. of all his cases were malaria patients —and that his treatment was not a purely anti-malarial one, his argument loses its significance.

The only valuable proof, namely, examination of the blood, is not stated as having been made.

The same holds good in regard to the cases of lymphatic-glandular inflammation observed by Ségard and Lesueur-Florent in Madagascar ; in some of these cases the enlargement was general, in others only the groin glands were affected. They were mostly accompanied by evening fever, loss of appetite and emaciation. In one case suppuration set in. Quinine, cinchona and iodide of potassium proved effective.

Of Lesueur-Florent's five cases which occurred on an insalubrious ship, one had the groin glands affected, three the femoral glands, and one both groin and femoral glands. The glandular inflammation came on suddenly, and one or several days after intermittent or remittent fever set in. The swelling was soft, elastic, and not at all painful spontaneously, and but slightly painful on pressure. At first the separate glands were swollen, but later on, in consequence of the participation of the periglandular tissue, the swelling at times attained the size of a hen's egg, and increased at every attack of fever and became somewhat painful. The fever disappeared after a few days under anti-malarial treatment (quinine, cinchona powder, arsenic), while the glandular enlargements abated, sometimes slowly, sometimes quickly. Lesueur-Florent is himself of opinion, however, that malaria only plays a subordinate part in the etiology of his cases.

According to my opinion these, as well as Martin's cases, most probably were climatic buboes. Perhaps this also holds good for the other cases of " bubo malaricus " observed (Bodnar, Ruber, Rotschuh)[1] (see p. 143).

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[1] The form of lymphangitis described by Roux (*Traité pratique des maladies des pays chauds*, iii., 1888, pp. 1-25) in which Ruge includes this ailment is, according to my

We have here an ailment that undoubtedly possesses a large geographical distribution, appearing to exist in Europe also, though having its principal distribution in East Africa, Madagascar, the East Indies, Sumatra, China, Japan, and the West Indies; some of the English statistics, however, evidently include buboes caused by injuries.

As to the etiology, Skinner is inclined, as he always observed intestinal disturbances in his cases, to associate the ailment with infection of the mesenteric glands. This view, however, finds no support from other observers.

Cantlie has pronounced another opinion on this disease, which he came across in Hong Kong. This author's view is that the buboes have some connection with plague and he identifies them with so-called *pestis minor*. In considering that disease (see p. 21), I have propounded the grounds on which it seems to me doubtful if the cases of disease thus designated have anything to do with plague, or if they are not probably identical with the climatic buboes which symptomatically resemble them.

In no case can pestis minor be made to include climatic buboes, as Cantlie strives to do. The objection raised by Godding that idiopathic buboes occur on the East African coast where plague does not exist is done away with by Koch's discovery of a plague centre in the interior of Africa, in Uganda. On the other hand, the cases observed by me in Japan in 1877-1881, long before plague was extant in China and India, absolutely exclude all connection with plague, and the same holds good as regards several other of the above-mentioned observations.

The question of the cause of climatic buboes, according to the material at present obtainable, is impossible to answer, and its explanation must be left for reply to future investigation. Only this much may be said, that the affection is caused by some still unknown factor that has undoubtedly some connection with climate.

In this sense the present designation, "climatic buboes," is unprejudiced and suitable until a better title can be found in substitution.

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opinion, erroneously placed. The mild form that mostly occurs on Réunion is undoubtedly a filarial disease, while I do not attempt to classify the severe form observed in Rio de Janeiro (see p. 143).

X.

LEPROSY.

DEFINITION.

LEPROSY is a chronic infectious disease, which for the most part is incurable, and is caused by a specific bacillus. In this disease more or less circumscribed neoplasms, tending to become granulomatous excrescences, develop; these are principally situated in the skin, in mucous membranes and in the peripheral nerves.

DESIGNATIONS.

The disease has a number of names which, originating from the most different countries and periods, mark its distribution in different regions and ages. The best known designation is *Lepra*[1] *Arabum* (*i.e.*, scriptorum) and *Elephantiasis Græcorum;* by the term lepra Græcorum psoriasis is understood, and under the term elephantiasis Arabum, the pachydermatous changes are comprehended. Of the other designations the following may be mentioned: *Sáraat* (Old Testament), *Morbus phœnicicus*, Hippocrates, Galen, Leuke (ancient Greek writers), *Vitilego* (Celsus), *Morphæa* (Oriental doctors of the Middle ages), *Maalzey* (oldest German designation), *Miselsucht* (obsolete German expression), *Mal mortuum*, *Mal morto* (Salernese), *Spedalsked* (Norwegian), *Spetelska* (Sweden), *Likthra*, from lik, *i.e.*, corpse and thràr, *i.e.*, rancid, or rotten. For nodular leprosy the synonyms are: *Lima fallassyki*, *i.e.*, the dismembering disease. For nerve-leprosy, *Holdsveiki*, *i.e.*, disease of the flesh (Iceland), *Leprosy* (Great Britain), *Melaatscheid* (Holland), *Lèpre, Ladrerie* (France), *Lebbra* (Italy), *Lova* (Greece), *Mal de San Lazaro, Gafedad* (Spain), *Gafeira* (Portugal), *Poklosság*, *i.e.*, the suffering of Hell (Hungary), *Guba* (Croatia and Montenegro), *Kuhsta, Raktapiti*, *i.c.*, black leprosy, *Kor*, *i.e.*, white leprosy (India), *Kiruën* (Siam), *Taikoh* (Chinese in Sumatra), *Fa-fung* (China), *Raibiyo, Kattai*, *i.e.*, disfigurement, and *Ten-kei*, *i.e.*, Heaven's punishment (Japan), *Mai-Pake*, *i.e.*, Chinese disease (Sandwich Islands), *Morfea* (Mexico), *Mal rouge de Cayenne, Kabobe* (West Indies), *Quigila* (Brazil), *Ngerengere* (New Zealand).

As may be gathered from the designations and descriptions which have been transmitted to us from ancient and mediæval times, many other chronic skin diseases, such as those of syphilis, lupus, scabies, eczema, psoriasis, &c., were confused with leprosy.

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[1] The word "lepra," according to Bloch, is derived from the Indo-Germanic root "lap" = to peel, and indicates a scaly and contagious skin disease.

HISTORY AND GEOGRAPHICAL DISTRIBUTION.
(See Map III.)

Probably Egypt, and more particularly the region of the Nile, is to be regarded as the home of leprosy; at all events this country at the most remote period was one of the principal seats of the disease. According to a papyrus discovered by Brugsch, the disease prevailed in Egypt 2400 years B.C., and according to Engel Bey, it was mentioned in a papyrus as existing there about 4260 B.C. Leprosy is also alluded to in the Old Testament. There it is mentioned in various parts under the name of sâraat (eruption, crushing blow), a disease which is minutely described in chapter xii. of the Third Book of Moses. Undoubtedly the most various skin diseases are here pictured, the differentiation of which has only been effected later, and amongst these, according to the description, leprosy is also included.

In India, and perhaps in China also, the disease has been known since ancient times, and it can be traced back in Indian inscriptions to 700 B.C. (Hirsch).[1]

In *Europe*, on the other hand, leprosy appeared later; the first account of its presence being in Greece, where it spread greatly during the two last centuries B.C. During the last century B.C., leprosy was brought to Italy by the troops of Pompey returning from Egypt; thence it spread over the greatest part of Europe, Roman colonists and soldiers carrying it into the countries invaded by the Roman legions, and the migration of people continued to disseminate the disease. Leprosy prevailed in Europe to the greatest extent towards the end of the thirteenth century, and was much contributed to by the crusades and the consequently increased commerce with the East.

Leper asylums were established everywhere and in these the unfortunate lepers, banished from human society, dragged out their miserable existence. This expulsion was conducted with a religious ceremony of the character of a funeral solemnity; for, in truth, henceforth the leper was dead to the outer world. Lepers were compelled to wear certain clothing and to carry a particular sign, more especially a rattle which announced their approach from afar. Should any person come near lepers he scrupulously avoided touching them, and people were even afraid that the wind blowing over these unfortunates could convey contagion. In the fourteenth century leprosy commenced to decrease gradually in Europe, and disappeared during the course of the century from our continent, with the exception of *isolated and mostly small centres of disease.*

These centres are in Portugal (especially the department of Lisbon), in Spain (especially in the province Valencia), in Brittany (in Paris also there is a large number of immigrant lepers), on the coast of the Riviera di Ponente, in Piedmont, the vicinity of Naples, Calabria, Apulia, Mark, on the Adriatic coast in the neighbourhood of Comacchio, in Elba, Sardinia, Sicily, Gozzo, Malta, Croatia, Dalmatia; on the island of Lissa; in Bosnia, Herzegovina, Montenegro, Turkey, Greece; on the Ægeian and

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[1] The disease sâraat has been variously described. Squire considers it especially to mean psoriasis, and Hebra takes it for scabies; Dunbar Walker considers it to be a disease no longer extant but resembling favus; Finlay and Proksch hold it to be syphilis; Sack, herpes tonsurans, and Münch is of opinion that it is vitiligo, known in Turkestan by the name of "Pjes." On the grounds of philological investigations Münch is of opinion that leprosy has not prevailed in Egypt since remotest times, but was probably imported thither from India, where it had existed for ages during the last centuries B.C.

Ionic Islands, Crete, Cyprus, in Servia, Bulgaria, Roumania, Hungary, Galicia, Poland, Bessarabia, Jekaterinoslaw, in the region of the Don, in Astrachan, Livland, Courland, Esthland, Finland, Sweden (especially in the province Helsingland; likewise, in Angermannland, Jemtland, Medelpad, Dalecarnia, Vermland, and on the islands Gotland and Oeland); in Norway, especially on the western strip of coast in the neighbourhoods of the fjords of Hardanger, Sogne and Förde, of the Söndmöre, in Romsdal, the domain of Throndjem, on the declivity of the Svartis, on the Lofotes, in the district of Tromsoe, and in Iceland, particularly on the south-west coast.

Quite lately a small centre of leprosy has also been discovered in Germany; this is situated in the region of Memel, and it was probably brought there from Courland at the end of the forties. According to Kirchner, there are 16 decided and 4 doubtful cases at Memel at the present time, and these originated from three centres, of which the first is situated in the suburbs of Schmelz, Sandwehr, Bommelsvitte, north and south of the town on the Baltic Sea and Courland Bay, and in the fishing village Melnerraggen. The second centre is formed by a group of villages at the north-east angle, and the third centre by another group of villages at the south-eastern angle of the district, close to the Russian frontier (Blaschko).

On the whole leprosy has gained some hold in Europe lately. Arning computes that the number of endemic cases in the western half of Europe at the present time is quite 3,000.

In *Asia* the region of distribution of leprosy is a very large one, and extends over the Caucasus, Asia Minor, Syria, Palestine, Arabia, Meso-potamia, Persia, Turkestan, particularly Bokhara, Samarcand, Miankal and Hissar; it prevails in India, Ceylon, Further India, the Malay Archipelago; in China, the Kwang-tung and Fokien provinces are the principal centres, and from these districts the disease has been carried by Chinese to the islands and coasts of the Pacific Ocean; in Formosa, the south of Corea, Japan (the Liukiu Islands are free from leprosy), East Siberia (Jakutsk), Kamtschatka, and the Aleutes, leprosy is met with.

Leprosy is also largely distributed in *Africa*. It is endemic in Egypt along the entire course of the Nile and along the coasts of the Medi-terranean and Red Seas. It exists in Nubia, Abyssinia, Darfur, Tripoli, Tunis, Algiers, Morocco, on the west coast of Senegambia as far as Cape Lopez (it has not been observed in Cameroon by F. and A. Plehn), in the Congo State, in South Africa, where it has lately increased; in Mozambique, Zanzibar, German East Africa; also, on the islands of Madagascar, Réunion, Mauritius, the Seychelles, St. Helena, the Cape Verdi Islands, the Canary Islands, Madeira and the Azores.

In regard to *America*, where, according to Ashmead, no leprosy existed amongst the indigenous population till after the appearance of the Spaniards,[1] leprosy now exists in New Brunswick, British Columbia,

[1] The Spaniards found *syphilis* in America amongst the native population, it, how-ever, only appeared in a mild form, as the natives had been inured to it for centuries. As the Spaniards were, however, unacquainted with this disease, whereas they knew leprosy well, they designated syphilis "lepra," mistaking it for a complaint akin to leprosy. Actual leprosy they called *malo de San Lazaro*, and lepers were named *Lazaros*. Later authors erroneously identified the Spanish comprehension of leprosy with true leprosy (Ashmead).

Lately, on the grounds of having discovered in Peru pre-Columbian clay figures with mutilated noses, upper lips and feet, some persons have come to the conclusion that leprosy existed in America before its "discovery." It is, however, by no means certain that the figures found are of pre-Columbian origin, and the mutilation repre-

a few spots of the United States, namely—Wisconsin, Iowa, Louisiana,
California, Minnesota, where the disease has been carried in by Nor-
wegians and Chinese. In Mexico the disease is met with; and in the
West Indian Islands (more particularly Trinidad, where leprosy was
unknown before the advent of the African negroes). In Honduras, Costa-
Rica, Columbia, Ecuador, Venezuela, Guiana, Brazil (in the provinces
of Para, Pernambuco, Bahia, Matto-Grosso, Minas-Geraes, San Paulo,
Parana), leprosy is known, being introduced there by negroes or Portu-
guese. In Paraguay, and the northern parts of Argentine and Uruguay,
lepers also exist.

In *Australasia*, New South Wales, Victoria, Queensland, Western
Australia and New Zealand, belong to the region of distribution of leprosy,
as do the following Islands of the Pacific Ocean: New Guinea, New
Caledonia, the New Hebrides, and the Fiji, Tonga, Samoa, Friendly,
Marquesas and Sandwich Islands.

Occasionally the region of distribution in the leprous countries is
confined to isolated, frequently very small, centres, while the remainder
of the population, though otherwise living under the same conditions of
life, are unaffected.

ETIOLOGY.

Leprosy is originated by a definite bacillus, the *bacillus lepræ*, which
was discovered by Armauer Hansen (1871), and more minutely studied by
Neisser (1879); the bacillus has hitherto only been seen in leprosy,
and indeed is found in all forms of the disease, but has never been
discovered in any other disease. This bacillus (see fig. 27, table I.)
forms delicate slender rods which are one-half to three-quarters the length
of the diameter of a red blood corpuscle; they bear a remarkable simi-
larity to tubercle bacilli; they also yield the same reaction of colour
as the latter, being stained a fine red colour with blue cytoblasts by fuch-
sine-aniline water, followed by acid treatment and contrasting dye with
methylene blue. They can, however, also be stained in simple watery-
alcoholic solutions of aniline dyes. According to recent investigations,
however, the latter method also succeeds with the tubercle bacilli.
There is therefore no essential difference of colouring between these two
micro-organisms, only a difference in degree; so that a few investigators,
such as Danielssen and Rake, are inclined to think them related, if not
identical.

Babes was able to confirm club-like formations and ramifications in the bacillus
lepræ resembling those of the tubercle bacillus; he therefore classifies both as
streptothricci.

Unna is of opinion that the micro-organisms of leprosy are not bacilli, but granular
threads, that is to say, globules connected together by chemical processes in masses of
filaments, which react differently, *i.e.*, of weaker colouring, and are therefore different.
He therefore suggests the term *coccothrix* for these microbes.

The bacilli lepræ (like the tubercle bacilli), as also the surrounding bacillar mucus,

sentations also do not resemble those caused by leprosy. The fact also remains that
the disease has never been seen on pure so-called Wild Indians. According to
Polakowsky (*Verh. d. Berl. anthropol. Ges.*, 1897), Jimenez de la Espada, the most
learned living authority of ancient Peru, connects the disease with one called *Uaga* or
Uta, an illness related to lupus, from which persons used to suffer in ancient times in
Peru, and which still exists in the deep, hot and damp valleys. It would be very
interesting to hear more on this subject, which has been also mentioned, but very
briefly, by Chastang (*Arch. de méd. navale*, 1897, Dec., p. 430).

contain *fat* (taking osmic browning deeply). Unna explains the specific conditions of the staining of the two kinds of bacilli from this circumstance.

Baumgarten, for the purpose of differential diagnosis, recommends that sections of tissue be placed in diluted alcoholic solution of fuchsine for twelve or fifteen minutes, then in acid alcohol for half a minute (one part nitric acid to ten parts alcohol) for discolouration, then to stain in methylene blue for two or three minutes, and finally to dehydrate in alcohol for three or four minutes. The bacilli lepræ stain well in this time, the tubercle bacilli, on the contrary, remain unstained. Similar results are yielded by staining the sections in Ehrlich's fuchsine solution for two or three minutes and bleaching them for half a minute or one minute in nitric acid and alcohol. The certainty of these methods is, however, disputed by Wesener and Wolters ; probably the age of the pathological process, duration and manner of the hardening, preservation, and the thickness of the section, may furnish elements which may eventually produce the opposite effect to the results mentioned.

Hansen and Looft lay particular stress for differentiation of the two bacilli on the fact that the tubercle bacilli are mostly found singly, while the bacilli of leprosy, on the contrary, are always found in *large numbers and stuck together in lumps and heaps* (like bundles of cigars). The most reliable signs of difference, however, are furnished by *culture* and *inoculatory experiments* on animals (guinea pigs and rabbits). The negative result of the latter method proves leprosy and the positive result confirms tubercle bacilli.

The bacilli lepræ, according to Cornil, may attain a far greater size, five to six times the length of those in the skin and mucous membranes, in parenchymatous organs, which, like the liver, are softer than the skin, and the same is the case in the lymphatic spaces of glands.

The bacilli are surrounded by a relatively broad mucus envelope which is observed most distinctly in dry preparations stained with watery aniline solutions.

They do not always become evenly stained but frequently exhibit an arrangement of the protoplasm resembling a pearl necklet. The unstained parts have been indicated by Neisser as spores. Probably, however, these are nothing but a disintegration of bacilli.

In fresh unstained preparations the leprous bacilli exhibit a lively *spontaneous movement* (they dart to and fro) and this is also observed in intracellular bacilli.

It is difficult to *cultivate* the bacillus lepræ artificially. Hitherto no success has been achieved in gaining cultures free from suspicion. It is true that investigators have cultured bacilli from leprous tissues and secretions, but it is doubtful if these are identical with the bacilli of leprosy. A number of observers (Bordone-Uffreduzzi, Gianturco, Babes, Levy, Czaplewski, Spronck, Barannikow, Teich) certainly appear to have obtained one and the same microbe in their cultures, and they all possess a certain fixity of decolouration.

The long discussion as to the *situation* of the bacilli in the tissues, carried on between Neisser and Hansen on one side, and Unna on the other, may now be satisfactorily decided by the fact that the position of the bacilli may be *intracellular* as well as *extracellular*. When free they may be observed, sometimes isolated, sometimes in groups. In the interior of cells they lie either in little heaps or they entirely fill the cell. In the uppermost strata of the neoplasms in particular, peculiar large round sharply bordered heaps, the so-called *globi*, are encountered ; these, when uncoloured, exhibit a wax-like polish, and stain almost homogeneously with aniline dyes. Opinions are divided as to the nature of these heaps, which are identical with the " yellow

flakes " described long ago by Hansen. According to this author these globi are nothing more nor less than exceedingly large leprous cells crammed full of bacilli (see below) ; according to Neisser they are agglomerations of leprous cells, whereas Unna, on the other hand, denies the cellular nature of the globi as well as of the leprous cells, and considers that they consist of heaps of microbes, which are kept together by masses of mucus and lie free in the lymph canals. Bergengrün and Gerick regard them as thrombi consisting of zoogloea, bacilli and coagulated lymph. In these heaps the greatest part of the bacilli have perished and are granularly disintegrated. In the globi as well as in the leprous cells it is not infrequently that marked spaces, *vacuoles*, are encountered, and these, according to Touton, represent liquefied parts of the cellular protoplasm that have been fed on by the bacilli, and which is perhaps mixed with a slimy excretory product of the bacilli.

The bacilli lepræ are *distributed to an extraordinary extent in the body of the leper*, and it is remarkable that often every reaction of the tissues is lacking in their vicinity.

The bacilli are found distributed in the tubercles and infiltrations of the skin and mucous membranes, more particularly in the freshly formed spots; also in the thickened nerves (also in the nerve fibres [Babes, Lie]), as long as the disease is recent, while in the further course of the process they are lacking. They are also found in the lymphatic glands, in the cartilage of the larynx (partly chains of cells filled with bacilli, partly free bacilli), in the cornea ; in the tubercles and interstitial infiltrations of internal organs, such as the lungs, liver (in the hepatic cells also, Cornil, Musehold), the intestines (Doutrelepont and Wolters, Schäffer, v. Reisner); in the testicle, and also in the lumen of the seminal ducts, where they lie in close masses [Neisser]; in the ovaries (Arning, Babes); in the eyes (Franke); in anæsthetic but not otherwise changed skin in nerve leprosy (Petrini). They have moreover been observed in and between the epidermal cells (Babes, van Haren Noman), in the hair follicles (Babes, Unna, Touton), in the hair sheaths (Touton) ; in the erectores pilorum (Touton), in the sebaceous glands, where they lie in the excretory ducts in large numbers (Babes), in the sweat glands, in and between the cells as well as free in their lumen (Touton), in the cellular connective tissue of the cutaneous nerves (Touton); in the Pacinian bodies of the skin of the palm of the hand and fingers, the central nerve fibres of which were in consequence destroyed (Sudakewitsch); in the spleen, lying partly free in heaps, partly enclosed in cells (Neisser, Leloir, Virchow); in the kidneys (Cornil, Babes, Rake, Lima and Havelburg) ; in the tissue of the spinal cord and brain (Chassiotis) ; in the Purkinjeian cells of the spinal cord and the spinal ganglion (Babes) ; in the ganglion cells of the sympathetic nervous system, whereas in its vicinity as also in the interstitial connective tissue no bacilli were found (Sudakewitsch); in the iris, ciliary bodies, choroid coat (Hansen and Looft), and in the retina (Neisser) ; in the muscles, in and between the cells of the interstitial connective tissue (Wunkow) ; in the tendons, and in their cellular connective tissue (Babes) ; in bone and periosteum (Sawtschenko), in the bone marrow (Bordoni-Uffreduzzi) ; in blood vessels, partly free, partly in white blood corpuscles, endothelial cells, and in the vessel walls, more particularly in the adventitia (Touton, Doutrelepont), as well as in the cells lying round the vessels (Babes).

The blood from healthy parts of the skin generally contains no bacilli, except during the acute attacks of fever, during which a dissemination and metastasis of bacilli takes place when they are found in the peripheral blood. This phenomena has been observed by Müller, Köbner, &c. Müller and others also found bacilli in the contents of *pemphigus blisters*, mostly in white blood corpuscles or in enlarged cells, very rarely free. Kalindero and others found the bacilli in *blisters artificially induced*, and Arning found them in the *inoculation pustules* of a tubercular case, whereas the inoculation pustules of patients of the anæsthetic form contained no bacilli.

The discovery of bacilli in the *secretions of disintegrated tubercles* (Neisser) is of particular importance, as also their discovery in the *secretion from the nose* (Bibb, R. Koch, Jeanselme, Kolle, &c.), in the *sputum* in tubercular affections of the palate, pharynx, larynx, lungs (Doutrelepont, R. Koch) ; in the *saliva*, in tubercles of the mucous membrane of the mouth (Leloir) ; in the *fæces* in leprous diarrhœa (Arning) ; in the *tears;* in *vaginal* and *urethral* secretions when the respective organs were affected (Besnier, Kalindero and Babes) ; in the *semen* (Besnier, K. Weber) ; in the *milk* in

tubercular leprosy (Babes) ; in the perspiration (K. Weber) ; in cast-off shreds of skin (Habel), and in scratched-off scales of skin (K. Weber.)

Schäffer has pointed out that the fine sprays of secretion from the mouth and nose during speaking, sneezing and coughing contain numbers of bacilli which may thus be distributed to a distance of $1\frac{1}{2}$ m. or even further.

The *secretion from the mucous membrane of the nose* plays the largest part in the distribution of the bacilli lepræ, for according to Sticker's investigations the nose is the part from which all leprous patients exude bacilli regularly, and mostly in enormous numbers, in their own immediate neighbourhood.

Sticker examined 153 patients, of whom $127 = 83$ per cent., had bacilli in their nasal secretions. Of these, 55 out of 57 patients had tubercular leprosy ; 45 out of 68 nerve leprosy, and 27 out of 28 patients the mixed form. The bacilli were found either in the purulent secretion of ulcerated or reddened and swollen patches, or in the mucus at the anterior part of the septum. The secretion most rich in bacilli was peculiarly viscid and mostly scanty. When bacilli existed in the secretion, there were mostly old, healed-over affections in the nose. In only 9 cases in which the nasal secretion contained no bacilli had the mucous membrane of the nose a healthy appearance. Kolle obtained similar results. He examined a total of 137 cases, of which $88 = 64\cdot2$ per cent., had bacilli in the nasal secretion. Of these, 45 cases were of the nature of tubercular leprosy ; all had bacilli in the nasal secretion. Of 30 cases of mixed infection, 22 had the same, and of 62 cases of nerve leprosy, 21 showed bacilli.

The difference in the quantity of bacilli in tubercular and nerve leprosy is remarkable and hitherto has remained unexplained. The tubercles and infiltrations of tubercular leprosy usually contain myriads of bacilli, while in nerve leprosy they are only found in small numbers in certain parts of the nerves or they may even be quite lacking. Perhaps in nerve leprosy the bacilli soon perish and their toxine plays an important *rôle* in the development of the disorders.

Arning, in Honolulu, found bacilli in great numbers in the putrid fluids of a cadaver that had been exhumed three months after burial. The bacilli, therefore, may live and multiply for this period in a climate such as that of Honolulu. Hitherto the search for the leprous bacillus anywhere but in the human body and its excretions and secretions has been in vain. It has been found neither in the dust of rooms, nor in the soil of houses inhabited by lepers, nor in tanks in which they bathe, nor in certain animals which have been handled by lepers, such as fish ; or in flies or mosquitoes caught in the mosquito nets surrounding the beds of bad cases of leprosy.

In order to absolutely confirm the specific signification of any sort of bacterium, it is necessary, according to Koch (1) to prove that the bacterium is always present in the disease to which it appertains, and occurs in no other disease ; (2) to culture the bacterium outside the organism, and (3) to again originate the same disease by means of the transmission of cultures. The first (and perhaps the second) *desideratum*, has been carried out in leprosy, the third, however, has hitherto not been fulfilled. Experiments on animals, also, which have been made by various authorities, by directly introducing pieces of leprous tubercles into the subcutaneous connective tissue, into the abdominal cavity, into the anterior chamber of the eye, &c., have been partly completely negative, or have yielded partly unsatisfactory, ambiguous results, such as local, leprous-like formation of tubercles, but no general leprous condition has been originated.[1] On the other hand a similar experiment by Arning was carried out with the desired result on a human being.

[1] Wolters gives a critical compilation of the experiments hitherto made.

A remarkably strong and healthy Hawaiian had been condemned to death for committing a brutal murder. On September 30, 1884, Arning, by permission of the King Kalakaua, inoculated the man, whose death sentence was commuted by his concession to this experiment, by making a deep skin incision on the left forearm, into which a freshly excised leprous tubercle was sewn. Four weeks after the operation rheumatoid pains set in in the inoculated arm, accompanied by painful swellings of the ulnar and median nerves. This neuritis disappeared gradually in the course of six months and a small leprous tubercle became manifest at the keloid-like, healed-up spot of inoculation. In September, 1887, true tubercular leprosy developed, it made rapid progress and led to a fatal termination six years after the inoculation.

This experiment, however, is unfortunately not quite free from objection, for it was conducted in a country infected with leprosy; the person experimented on had formerly lived amongst lepers, and as was pointed out later on by the doctor of the Molokai leper asylum, Dr. Swift, his family were afflicted with leprosy, several of his maternal relations as also a brother of his wife, suffering from leprosy. At the same time, compared to the usual duration, the short period of incubation is remarkable.

In Coffin's statement on leprosy in Mauritius and Réunion, a somewhat similar case is reported. It is customary in these islands to make use of the prisoners in the house of correction to attend the patients in the leper asylum. One poor prisoner who had formerly been in the leper asylum preferred being there to detention in the house of correction. He therefore wounded his right forearm with an instrument which he had previously dipped in pus from the wounds of a leper. Nevertheless he was sent to the house of correction. Two years subsequently his wish was fulfilled, and he returned to the leper asylum with fully developed nodular leprosy, which had started at the inoculated spot and to which he succumbed later on.

Earlier experiments of transmission have, however, been attempted on man. Between 1840 and 1860 Danielssen conducted a series of inoculations on himself as also on others (Kaurin), and recently Profeta inoculated himself and also a few medical students; Jitsch also inoculated several persons. All these experiments, however, had negative results.

Cornil, on these grounds, conjectures that the material from skin nodules and other leprous neoplasms hitherto used for this purpose is not suitable, as the bacilli contained in the tubercles have already died off.

But even without confirmatory proof of experimental transmission, the constant bacillary condition leaves no doubt as to the infectious nature of leprosy. This opinion naturally leads immediately to the further question as to whether this disease be *contagious* or not; opinions in regard to this question have changed in the course of time. In the middle ages leprosy was universally considered to be infective, and it was this belief that led to the expulsion of those afflicted from human society and to the erection of leper houses. At the commencement of the nineteenth century[1] the contrary opinion gained ground and Danielssen and Boeck's theory of heredity predominated. Since the discovery of the

[1] A short essay on leprosy written in the latter half of the eighteenth century (G. G. Schillingii de Lepra commentationes, Lugd. Batav., 1778), by a German doctor who gained his knowledge of leprosy in Surinam, is highly interesting, as the author's views on the contagiousness of leprosy are nearly akin to our modern opinion. In the chapter dealing with " De contagio lepræ," the author delivers himself as follows: " Superfluum videri posset de contagio lepræ disputare de quo nemo fere dubitat . . . Stat igitur sententia, contagiosum esse lepræ virus, atque de parentibus in liberos, de nutricibus in alumnos, de conjuge in conjugem transire; quin etiam persuasum habeo ex diuturno contubernio absque intima illa corporum miscela per spiritum oris et hiscina ulcerum effluvia hanc luem cum aliis communicari . . . Scilicet minima

bacillus of leprosy, however, a revolution has set in and the opinion that leprosy is infectious now numbers most followers.

The fact that in recent times and in various countries which are not old endemic seats, a large and rapid spread of the disease has taken place, seems to confirm the contagiousness of leprosy and its distribution by means of human intercourse.

The Sandwich Islands furnish a case in point. Though Hildebrand's statement that the disease had been carried thither by Chinese in 1859 has not been confirmed, and though according to Arning's minute investigations it has been endemic there much longer, yet it was of very rare occurrence, and it only began to spread more quickly about the end of the fifties or the commencement of the sixties. In 1866 the Government found it necessary to adopt isolatory measures and to have 400 lepers exiled to the little island of Molokai. In 1881, the number of patients there had increased to 800, but in addition there were so many lepers on the remaining islands, that their number was computed at 4,500, *i.e.*, one-tenth of the entire native population; during the last fifteen years about 2,000 lepers have died in Molokai. Tryon states that under the influence of leprosy the number of natives has suffered a diminution of 7·7 per cent. during the six years, 1872-1878.[1] Such extensive strides of a disease can scarcely be explained otherwise than through contagiousness, and in addition the conditions of life of the Sandwich islanders have undergone no changes. The customs and habits of this people are such as to favour the spread of an infectious disease. They live crowded together in small hovels, they use in common the same utensils for eating and drinking, and the same pipes; they lead a dissolute life, and have no fear of the disease, so that cohabitation and marriage between diseased and healthy is no rarity (Neisser). In 1868 vaccination was introduced, and the careless transmission from arm to arm appears to have essentially contributed to the spread of leprosy, a statement that is borne out by the proof of the presence of the bacillus of leprosy in the inoculatory pustules, as observed by Arning and others.

New Caledonia may be quoted as a further example. Grall reports that leprosy was introduced there about 1860, having been carried thither by one or several Polynesians. At first it spread slowly, but later on more quickly, amongst the indigenous population, so that at present a large portion of them are afflicted with the disease, and between 1890 and 1892 it was found necessary to erect three leper asylums. The neighbouring islands were also infected from New Caledonia. Thus the disease was carried to the Pine Island by an exile, and there spread first of all in the exile colony, where it appeared in the family where the first patient lived, and then amongst the natives. Of these the interpreter was first attacked, as in consequence of his knowledge of languages he had most communication with the exiles. Of the latter fifty-six have died from leprosy, and nine of the natives have either fallen ill or died. On Mare Island (belonging to the Loyalty Islands) the disease was first observed in a Protestant convert who had lived in Guinea many years; since then leprosy has only spread amongst the Protestant part of the population, whereas the Catholic part, which have little to do with them, have remained relatively free.

At the end of the eighteenth century a leprous passenger was landed from a ship on Mauritius. Ten years later there were many lepers on the island, and about the middle of the nineteenth century they had become so numerous that a leper asylum had to be founded. The Island Rodriguez was infected by a fisherman who was diseased when he came over from Mauritius to settle (A. v. Bergmann).

miasmatis particula et pene dixerim atomus si corpus sanum, quocunque demum modo, intraverit, ad morbum producendum sufficit. Habet enim lepræ virus, sicut cætera contagia, vim quasi fermenti, atque totam humorum massam per intestinum quemdam motum sibi assimilat. Qua propter non dubito, quin etiam perinde ac venenum variolarum et scabiei per insitionem propagari posset. Notandum autem est, infectionem non pendere a sola miasmatis efficacia, sed multum etiam facere temperaturam corporis. Hinc quemadmodum videmus nonnullos homines veneno pestis, variolarum, scabiei diu resistere, sic quoque fieri potest, ut homines quidam cum leprosis diu impune versentur, et vel intimo misceantur commercio, nec tamen leprosi evadant. Facit huc, quod in scholis vulgo dicitur: non solum activititatem causæ morbificæ, sed imprimis receptivitatem corporis considerandam esse."

[1] Alvarez asserts that between 1866-1894, the number of natives in the Sandwich Islands decreased from 58,765 to 38,512, and he computes the number of deaths from leprosy at 5,000. He, however, only to a slight degree lays the blame of the decrease of the population on leprosy; other factors, above all, the medicine men, syphilis and the abuse of alcohol and opium, are responsible.

Zuriaga reports that leprosy was carried into Parcent, a village in the province of Alicante, Spain, in 1850, by a leper who came from the Philippines, and as no protective measures were taken the disease spread, so that in this little spot there were in 1888 sixty lepers, of whom forty-five died and fifteen were still living.

Vignard reported in 1876 that leprosy had been introduced into Kedrille, a fishing village situated at the mouth of the south arm of the Danube, on the Black Sea, by a leper seventeen years previously.   The disease spread gradually and chiefly affected entire families.

In Livland, where leprosy had died out more than two centuries ago, the disease again appeared in the middle of the nineteenth century; it cannot, however, be distinctly ascertained whether this misfortune was in consequence of the increased commerce with Norway, or through having been carried in from the Crimea or other leprous countries by home-coming soldiers.   However, since then it has gained a firmer foothold, so that at the present time there are more than 100 lepers in Riga, that is to say, one to almost every 2,000 inhabitants.   In two almshouses in Riga containing 340 inmates, v. Reisner found twenty-two lepers. Of these four had been diseased previous to their admission to the institute, nine had been in beds next to patients suffering from leprosy, five had had lengthy intimate companionship with lepers, and only four cases could be relegated to incidental infection.   Not one of the patients came from a leprous family.   A. v. Bergmann compiled 108 cases, and in 60 per cent. of these he was able to trace certain or probable infection.

A fact that likewise speaks strongly in favour of the theory of the capacity of infection of leprosy, is the circumstance that *in recent times leprosy in different countries has considerably decreased under the influence of the introduction of isolation of the afflicted.*

Thus in Norway since about 1859, from which period there has been stricter isolation of lepers, their number has diminished.   In 1856, when the doctors first computed their numbers, there were 2,833, and in 1895 only 688, so that in recent years two out of the five leper asylums could be closed.   According to Hansen's computation Norway may be, roughly speaking, quite free from leprosy in about 1920, if the decrease of lepers continues in the same degree (Holst).

In the Caucasus Macnamara reports that since 1841, when isolation was there established, the lepers are considerably reduced.

Neisser mentions that in the West Indian Island, Curaçao, where strict isolatory measures prevail and immigrant foreigners are subjected to supervision, leprosy decreases year by year; whereas in Trinidad, a neighbouring island possessing the same climatic and social conditions, but where such measures are not adopted, leprosy steadily increases.

The same conditions, according to Kaurin, obtain in Guiana.   In Dutch Guiana, where lepers are strictly isolated, there is but little leprosy, whereas in the French and English parts of the country, where isolation is regarded as a barbarity and an unpardonable restriction of personal liberty, the number of lepers is considerable, and has augmented during recent years.

The expulsion of lepers from human companionship also plays a large part in the disappearance of leprosy from Europe in the sixteenth century.

In isolated cases it is often very difficult to trace the source of infection, and this is not surprising when one takes into consideration that the etiology of many cases of diphtheria, scarlet fever, cholera, &c., remain unexplained, notwithstanding their sudden outbreak and their short period of incubation, whereas in leprosy years may elapse after the infection before the first symptom of disease sets in, and then only very gradually.   However, there are a great number of cases in the literature in which transmission of the disease can be positively traced, and of these a few examples are here given.

Hawtrey Benson's case is one of the most convincing.   This observer, in 1872, exhibited to the Dublin Medical Association an Irishman suffering from nodular leprosy, who had lived in the West Indies twenty-two years and there acquired the disease.   After having been under treatment in hospital for a few weeks he returned to his native land and there died about eleven months after.   The patient's brother slept in the same bed with him until shortly before his death, and wore his clothes. This man had not left Ireland, where leprosy is unknown, for forty-six years, had

only once been in England, and no other case of leprosy had occurred in his family. In 1877 he was shown at the Dublin Medical Association, also suffering from tubercular leprosy.

Father Damien de Venster, who came from a Belgian family, in which leprosy had never occurred, went to the Sandwich Islands in 1873 in order to devote himself to the service of the lepers, with whom he lived intimately associated for many years in the leper asylum in Molokai. In 1882 he exhibited the first symptoms of leprosy, and in July, 1889, he died from this disease (Macnamara).

Kaurin, in 1886, had under observation in the Reknä Hospital in Norway, a boy, aged 9, afflicted with tubercular leprosy. The lad fell ill after sleeping for years in the same bed as his great uncle, who was leprous, and subsequently died. The parents, grandparents, and four sisters and brothers of the boy, none of whom had slept near the great uncle, were free from leprosy.

Lorand mentions a case from Sweden, a soldier who had just left the service, bought and wore the clothes of a leper who had ulcerated nodules on the legs. The soldier wore the clothes and subsequently developed leprosy, and likewise had nodules on the lower extremities.

Another case communicated by the same author was observed in Norway (Dr. Thorp). It related to the daughter of a peasant living in a lonely valley, who suffered from nodular leprosy. Five or six years previously a servant was engaged in this house, and it being found he was leprous, no one would go near him, and the girl nursed him. Not another single case of leprosy had occurred in this remote valley for fifty years.

Hellat reports that a woman, not afflicted by hereditary leprosy, and who lived in a district of Russia, in which cases of leprosy had not occurred within the memory of man, fell a victim to leprosy three years after the return of her son, who had been in service by the Caspian Sea and had there acquired leprosy, having been in close association with lepers whilst residing there.

A. v. Bergmann quotes the following cases. The only daughter of a judge was attacked by leprosy, and later on it was found that she had often bandaged ulcers on the legs of her maid, who subsequently died from leprosy in the hospital in Riga.

The daughter of a major fell ill from leprosy which she acquired from a leprous child who attended a sewing school kept by her. Afterwards the mother became infected through nursing her daughter.

A juggler, who only visited places free from leprosy, but who for a long time had a travelling companion who was obviously leprous, exhibited typical leprosy three years after parting from him.

Lokh has made valuable investigations as to the etiological connection of isolated cases of the disease on the island of Oesel (Livland). In all the cases quoted the persons infected had been *long and intimately associated* with the lepers, and such close connection is absolutely necessary for transmission, as the virus of disease is not easily communicated, and the contagious character of leprosy is therefore not so very great; the disease is generally far less infectious than syphilis, and probably also less than tuberculosis.

The argument brought forward against the possibility of infection of leprosy is the fact that in marriage one of a couple is very frequently leprous without infecting the other, and that it is exceedingly rare that the disease is observed amongst the doctors and attendants at leper asylums.

In 1882 I visited a leper house in Hendella, near Colombo, in Ceylon, which had already existed more than a century, having been built before the period when Ceylon passed into the possession of the English from the Dutch in 1796. For generations the offices of sick attendants have been handed down to certain families living on the premises, and yet I was assured by my conductor, a doctor, that no case of leprosy had ever occurred amongst them.

The same, however, is also the case in other contagious diseases. Transmission seldom takes place in the marriage of tuberculous persons, and cases of infection are very rarely observed in the syphilitic wards of hospitals. Nobody will assert that these two diseases are not contagious. It must also be added that contradictory observations in regard to leprosy have been made. Thus Emerson, in 1888, by desire of the Government of Honolulu, instituted enquiries on the subject and found that of 66 so-called kokuas, *i.e.*, male and female attendants on lepers on Molokai Island (who were as a rule married to the patients), 39—59 per cent.— became leprous after a stay of from two to fifteen years, 11 were doubtful and 16 not leprous.

On the whole the contagious nature of leprosy in different countries is not similar, appearing to be greater in the more recent centres of leprosy than in those where leprosy has been endemic for ages. Perhaps in the course of tens of centuries the virus of disease has decreased in virulence, or by the destruction of the most susceptible individuals a natural immunity may gradually have been formed.

In regard to contagion, the nodular form appears to be more dangerous than the anæsthetic form, and this may be explained by the fact that in the nodular variety there are myriads more bacilli than in the anæsthetic, in which also there are no secretions containing bacilli. Hansen, by means of statistics, proved that the increase of fresh cases of leprosy is greatest in those districts of Normandy where the most nodular cases occur.

The transmission of the disease takes place from man to man, directly or indirectly. The different secretions and excretions of lepers in which, as mentioned above, the bacilli of leprosy are found, may become the carriers of the virus of disease. Transmission may also be effected by the use in common of utensils for eating and drinking, wash-tubs, towels, clothes and the like (see Lorand's case mentioned above; similar cases are also related by Hansen and Looft). Transmission by means of insects such as flies, bugs, mosquitoes, is also possible. We do not know whether the bacilli possess such a power of resistance that they are capable of existing outside the living human body for any length of time, and if when they again invade the body later they can originate the disease. Geill is of opinion that the bacilli go through certain stages of development in the soil before invading the human organism.

The introduction of the bacillus lepræ into the human body may probably be effected in different ways. *Injuries to the epidermis* is one of these. Peters states that leprosy occasionally sets in locally after injuries, such as a cut on the finger or an injury to the feet on rough, sandy soil.

The *mucous membranes*, more particularly the *nasal mucous membrane*, form another point of entrance. Sticker is even of opinion that in leprosy, as in chronic glanders, the primary effect has always its seat on the mucous membrane of the nose, and that leprosy therefore primarily is a nasal disease in a still more limited sense than syphilis is first a sexual disease, and tuberculosis a disease of the apices of the lungs. The lymphatic glands of the nasal mucous membrane are connected with those of the skin, with those of the sub-arachnoid spaces of the brain, and with those of the spinal column and the perineural sheaths of the peripheral nerves; by these channels the bacilli are able to spread through the entire body.

Perhaps the invasion of the bacilli may also take place through the *sebaceous glands, hair follicles*, and *sweat glands*, in which and in the vicinity of which, bacilli are frequently found, or they may perhaps

penetrate by way of the *respiratory and digestive organs.* Kolle states that Black was able to prove that in the early stage of nodular, as well as of nerve leprosy, the spleen and liver may be crammed full of bacilli while the first changes of the skin are scarcely perceptible ; this speaks strongly for an infection through the digestive tracts.

As leprous spots have also been observed on the genitals, transmission of the disease *through sexual connection* is also possible.

After their entry into the human organism, the bacilli pause in certain localities, perhaps the lymphatic glands, and undergo a period of incubation, and subsequently spread through the body principally by way of the lymph passages, more rarely by means of the blood.

It has already been mentioned above that *vaccination* seems to have played a large part in the spread of leprosy in the Sandwich Islands. The possibility of such a manner of transmission, even at a time when no pronounced symptoms of the disease are present, is proved by the cases communicated by Gairdner and Daubler.

According to Gairdner a doctor in an English colony vaccinated his child with lymph taken from a boy in whose family there had been leprosy, but who only himself became leprous subsequently. The doctor afterwards vaccinated the child of a Scotch captain whose vessel plied between Scotland and this colony from his own child. Both children became afflicted with nodular leprosy. As leprosy is not rare in the colony where the doctor's child lived, it is not impossible that this child may have become infected in some other way. But this is hardly probable with the other child, who only periodically came to the colony.

Däubler, in Robben Island, South Africa, saw two women to whom leprosy had been transmitted through re-vaccination. In the case of the one woman no pustules developed on the places of inoculation, but they became very much swollen during the course of the next fortnight, while the patient often had evening fever and felt languid. The places became brown and this discolouration gradually spread over the skin of the entire upper arm and the upper third of the forearm. In the twelfth and fourteenth week after the vaccination the patient had several severe rigors and soon after brownish spots appeared on the skin of the cheeks and forehead. Soon after tuberculous prominences developed on the forehead and pronounced lepra tuberosæ developed. The course was quite similar in the case of the other woman, who was re-vaccinated at the same time as the woman above mentioned and by the same doctor. The person from whom the lymph had been taken for both women had meantime died from nodular leprosy ; she came from a family in which the disease had already occurred, a circumstance not known to the vaccinator.

Objectors to vaccination have availed themselves of the part played by vaccination in the dissemination of leprosy and to exaggerate the possibility of infection. In their blind zeal they have even gone so far as to assert that leprosy, owing to vaccination, has increased almost everywhere. It was for this reason that Hansen in 1891 addressed to every doctor in Norway the question as to whether in their practice they have come across a case that could be traced to vaccination. No case of the kind was recorded, although vaccination has been obligatory in Norway for a long time, and lymph from children of leprous families must frequently have been taken. As little children are very rarely leprous it is explicable that leprosy has not been carried in this way. In India, also, according to the Report of the Indian Leprosy Commission in 1890, vaccination against smallpox has never led to the transmission of leprosy.

In medical literature different cases are mentioned in which leprosy developed in *conjunction with a syphilitic infection,* and I myself observed a case of this kind. This may raise the question as to whether the individual afflicted with both diseases may simultaneously transmit a syphilitic virus with the virus of leprosy.

The *incubation* period in leprosy may last for years. This is proved in the case of patients who several years after leaving leprous countries develop the disease.

A. v. Bergmann has, from the summing up of all communicated observations, come to the conclusion that the average period of incubation is three to five years, this being the period between the intercourse with lepers and the appearance of manifest symptoms of leprosy, and therefore comprising the stage of incubation and prodroma. Impey believes that incubation in the multiplicity of cases does not exceed two years. Cases with periods of incubation of ten, fifteen, twenty years, or even longer, have been communicated. Hallopeau reports a case in which the period was thirty-two years, but these should be regarded with scepticism, as the patients during these long periods of incubation were not carefully observed, and isolated eruptions, which might easily have escaped the attention of such persons for years, may frequently precede other and more perceptible symptoms (see below).

The question of the *heredity* of leprosy stands in a certain antagonism to that of the contagion of the disease. Those who deny the contagiousness favour the theory of heredity. Danielssen and Boeck especially favour the opinion of heredity from the father's side. The assumption of inherited transmission is founded on the circumstance that a large percentage of lepers have parents, sisters and brothers or distant relations who are likewise leprous. This fact, however, is equally well explained by *infection through the particularly intimate family intercourse*. Leprosy is a family and house-disease, or, as expressed by Dehio, a disease of the household and of close intimacy.

When the members of a family are living apart the seeming influence of heredity, as Hansen remarks, is not observable. In the city of Bergen there are thousands of persons who originally came from leprous districts where they have leprous relations, yet they themselves never become leprous. The same applies to the Norwegian settlers in America, of whom many came from leprous districts, yet not one developed the disease. On the other hand, in Norway about from one quarter to one-fifth of all lepers have no leprous relations; in these cases, therefore, there can be no question of heredity. According to the observations made in India only from 4 to 8 per cent. of the children of leprous parents become leprous in their turn (Azoulay.) The following figures are likewise confirmatory :—

Ehlers examined 119 cases in Iceland whose family history could be minutely traced, as the Icelanders have complete tables of their pedigrees. Of 3 of these both parents were leprous, of 15 the father only was a leper, of 4 the mother only was leprous, and of 20 the brothers and sister were diseased.

The 266 leprous parents at present resident on Robben Island have 951 children, of whom only 23, that is less than 3 per cent., are lepers. Of the 520 inmates of the leper asylum, 475 were the children of healthy parents, of the remaining 45 the father only was leprous in 25 cases, the mother only in 16 cases, and both parents were leprous in but 4 cases (Impey).

The above-mentioned examples of contagion declare against the heredity of the disease, as well as the following facts :—

(1) *The lack of a fœtal form* (in contradiction to syphilis).—A few observers, notably Zambaco, state that they have observed signs of leprosy at birth, or a few days to months subsequently, but these cases are by no means assured. The possibility of hereditary transmission in the sense of an intrauterine infection must, however, be conceded. In

view, however, of the long period of incubation of leprosy, it can hardly be decided whether it is intrauterine infection or whether the infection was transmitted during the first few months after birth.

(2) *The marked lesions of the generative organs* in both sexes which set in early in the disease, so that the sexual functions of the patients are soon diminished or extinguished, also declare against heredity. It has been observed in India that almost two-thirds of the marriages of lepers are childless (Azoulay). Should leprous women conceive, they mostly miscarry, according to Zambaco, in the third or fourth month of pregnancy, or the children are born cachectic and soon die.

(3) *The rapid disappearance of the disease*, as observed in a few regions, such as in the Faröe Islands and on the coasts of the Bohuslän in Sweden (Hjort), tend to nullify the belief in heredity.

Probably, however, the *pre-disposition* to leprosy is *hereditary*, that is to say, there is but a small power of resistance to the invasion of the bacilli. Kaurin considers there is a hereditary susceptibility from the fact that when one of a married pair is leprous, the other sometimes remains free from the disease and is sometimes infected; in the former case he believes that there is no predisposition and in the latter that there is. von Blaschko supports this opinion from the fact that leprosy is more easily transmitted to blood relations, children and sisters and brothers, than to husband or wife as the case may be.

Before the discovery of the bacillus of leprosy the cause of the disease was sought for in the most diverse conditions. A glance at the geographical distribution of leprosy will show that the disease occurs under the most varying terrestrial and climatic conditions, but a predilection for coast regions and islands is apparent. It was therefore thought that, as in malaria, great *moisture of the soil* had an influence in the development of the disease. Moreover a great significance has been ascribed to the *alimentary conditions*. Partaking of salted, rotten, or of certain fish—recently the fish theory has been brought forward again by Hutchinson—the inordinate eating of fats or rancid oils, the immoderate eating of pork, the eating of bad cheese, bad sorts of flour, putrid olives or other raw foods, want of salt in the food, have all been assumed to be causes of the disease, without any proof whatever.

Race plays an important part in the etiology of the disease. In countries with a mixed population the white race is far more rarely attacked than the coloured, especially the blacks. In half breeds the immunity is decreased.

Besides the difference of race, the *hygienic conditions* under which the people live, as well as the *intercourse* they have *with the infected part of the population*, come under consideration. According to Munro the Arabs, for instance, in the Malay Archipelago, are wont to be spared, while in Algiers they are more frequently attacked than the Kabyles.

Reports from all leprous countries coincide in stating that the *male sex* exhibit a greater predisposition to the disease than the female.

In regard to the *time of life*, the disease develops most frequently between the 15th and 30th year. Leprosy, however, spares no age, with the exception of the first years of life; it rarely appears before the 3rd or 5th year. Bidenkap observed two leprous children aged between 2 and 3 years.

Constitution exercises no influence, but the *predisposition* is *individually different*. Isolated persons seem to enjoy complete immunity. R. Koch furnishes the following examples:—

A woman in the circuit of Memel first lost her husband and then four grown-up children from leprosy. She had nursed them all and during nearly twenty years was in intimate association with lepers, yet she remained quite healthy.

For twelve years there was leprosy in a man's family, and for years he shared the same bed with his leprous wife without acquiring the disease.

In infected districts the disease generally appears more frequently in the country than in the towns. Though riches and good living by no means exclude the occurrence of leprosy, it is the lower classes and the poor living in dirt, misery and want, who are principally subject to the disease. Deficient care of the skin, personal uncleanliness, dirty and miserable condition of the dwellings and clothes, and close quarters of the inmates, all undoubtedly play an important part in the spread of the disease, for reasons readily understood. They also contribute to the fact that the contagiousness of leprosy varies in different countries and in different nations. Thus in Japan, the population of which are a cleanly nation, infection, according to my experience, is but slight, and although lepers there have not been isolated for ages, dwelling with them has not had the injurious consequences in Japan that it has had in other countries. The cleanliness in towns is even greater than in the country, and correspondingly leprosy is more frequent in rural districts, the villages of the Eta—the Japanese pariahs which are notorious for their dirt—are particularly centres of leprosy. In Constantinople, according to v. Düring, leprosy has been particularly observed amongst the Spanish, who live under inferior hygienic conditions to the Turks and Greeks.

Hansen attributes to the cleanliness of the descendants of Norwegian lepers who emigrated to America (see above), the circumstance that not one of them became leprous. " The first thing learned by the none-too-clean Norwegian peasant over there is to keep himself clean."

It is certainly also not by chance that the disappearance of leprosy from Europe was simultaneous with the introduction of better hygienic conditions, especially with the increase of cleanliness and the adoption of the shirt and chemise as a universal article of clothing ; these garments in mediæval times having been regarded as merely an article of luxury.

SYMPTOMS AND VARIETIES OF DISEASE.

The signs and symptoms of leprosy depend on the seat of the leprous neoplasms. The symptoms differ according as the neoplasm is situated in the skin, the mucous membranes, or peripheral nerves. These differences in the aspect of the disease have led to the recognition of two forms of leprosy, *nodular leprosy* and *nerve leprosy*. These terms originated with Danielssen and Boeck, the founders of the scientific study of leprosy. These two forms, though correct from a practical standpoint, are nevertheless not strictly divided one from the other, for they frequently overlap, the symptoms of one form being often combined with those of the other during the course of the disease, or even from its commencement. It is very seldom that quite pure cases of one or the other form are observed ; the majority belong to the *mixed form*. I consider it unjustifiable to differentiate further forms according to the prevalence and succession of particular symptoms as various authors have done.

1. Nodular Leprosy.

(Lepra tuberosa, L. tuberculosa, L. tuberculata.)

(See fig. 28, table III.)

The disease, as a rule, but by no means constantly, is ushered in by *prodromal* symptoms. These are exceedingly manifold, and consist of universal languor, indisposition, and an intense feeling of cold, which is experienced sometimes over the entire body but more frequently only at the extremities, especially the hands and feet. The feeling of cold is particularly severe in winter, and is then often combined with the feeling of formication and numbness. One frequent sign is a tendency to perspire profusely all over the body, more particularly on the trunk. Such conditions as heaviness and dragging of the limbs, pains in the back, headaches, sleepiness, giddiness, loss of appetite, nausea and vomiting, digestive disorders, and above all, attacks of fever that exhibit sometimes an intermittent, sometimes an irregular, character, are occasionally complained of. Several authors state that nasal lesions are amongst the first signs of disease, and consist of an unpleasant sensation of dryness and tickling in the nose, stopping up of the nostrils, bleeding from the nose, and violent headaches radiating from the root of the nose.

Blaschko, with justice, throws doubt on the belief that these symptoms, which undoubtedly indicate a constitutional general illness and universal intoxication, are really the very first symptoms, for before such effects could be experienced the bacilli lepræ must be established in the organism in great profusion. Probably these symptoms are preceded by manifestations in the skin or mucous membranes that have been unremarked by the patients. The nasal symptoms are certainly attributable to lesions in the mucous membrane of the nose. Sometimes the disease begins with isolated eruptions which may alone persist for years (A. v. Bergmann).

After these symptoms have gone on with interruptions for months or even years, red *spots*, which are usually somewhat raised, break out, especially on the face and extremities. These spots are at first hyperæsthetic, or cause itching. The eruption may again disappear, only leaving the remnants of pigmentation behind or even without leaving a trace, or they become transformed into *nodules* which gradually become larger, becoming either more elevated or larger in circumference. Neighbouring nodules may become confluent and in this manner cause extensive *infiltrations*, on the top of which again other nodules appear.

Usually the nodules are situated in the cutis, sometimes they are deeper-seated in the subcutaneous connective tissue; in the latter case they do not protrude above the skin, and can only be perceived on passing the hand over the skin. The size of the nodules varies. As a rule from the size of a lentil to that of a hazel nut, they may by confluence become as large as a walnut or even larger. Their colour generally is dark red, later on they become brownish-yellow or assume a greyish slate-coloured tinge ; in the dark races they appear yellower than the surrounding skin. They exhibit a wax-like polish and a fine vascularisation, which is always found on minutely examining them (A. v. Bergmann). The surface of the macula exhibits a slight exfoliation, and sometimes, when situated on the nose, an eczematous appearance, for it becomes moist and scabs are formed. As to the consistency of the nodules, at first they are usually soft and become harder later on. On trying the sensibility in the region of the nodules and infiltrations anæsthesia is apparent.

According to Unna the nodules appear ochre-yellow under the diascope, whereas lupus nodules exhibit a deep yellowish-brown tint, and syphilides a delicate greyish-yellow tinge.

The formation of nodules takes place either slowly, little by little, or, having been preceded by *erysipeloid redness*, often lasting several days, they appear all at once in great numbers on one part of the body. The part in question becomes red and swells, with the accompaniment of high fever; simultaneously the corresponding lymphatic glands become enlarged and painful, and when these signs have receded the new eruptions are observed. The same part of the body may, in this manner, be attacked several times consecutively.

Unna differentiates different *forms of nodules* :—

(1) *Subcutaneous lepromata*, in which slightly raised swellings and diffuse infiltrations, by which the intact cutis is raised and stretched, form the principal feature of so-called nodular leprosy.

(2) *Nodules appearing directly within the cutis*, which do not often mix with the first form but mostly appear as a distinct form.

(3) The *acute inflammatory skin nodules* which, caused by embolism of the vessels through bacilli. appear with symptoms of fever and have their seat in the cutis and hypodermis. They resemble erythema nodosum, but are less sharply circumscribed, and are lost in inflammatory œdematous surroundings.

On the other hand, however, it is possible that local healings take place under the influence of the erysipelas described ; the nodules disappear leaving white or dark spots ; nevertheless the formation of new nodules at other places still goes on. Temporary absorption of all or part of the nodules is often observed during the course of an intercurrent acute illness, such as an exanthematous fever, or during an exhausting disease such as phthisis.

Softening is another change to which the nodules may be subjected. They commence to fluctuate and finally break open, and flat *ulcers* ensue with sharp borders and smooth, unhealthy granulated bases which exude a little thin pus that dries up into crusts and scabs, and frequently exhibit a slight tendency to heal. The ulcers are indolent and gradually become less and less sensitive, and even when they do heal up anæsthetic cicatrices are mostly left. The cause of the softening and ulceration of the nodules is often ascribed to mechanical causes. The legs are particularly liable to become thus ulcerated, due to the disorders of circulation in the lower extremities.

When the illness is of long duration *shrivelling* of the nodules and infiltration sets in. They assume a light yellowish tinge and have a fibrous appearance ; nevertheless they never shrivel up entirely (A. v. Bergmann).

The parts of the body most frequently attacked by the nodules are the *face* and the *extremities* ; on the latter the extensor aspects are affected, the knees, elbows, hands and fingers being most severely attacked. It is but very rarely that the hairy parts of the head are affected (Westberg, Blaschko, A. v. Bergmann), or the palm of the hand (Blaschko), the soles of the feet, or the glans penis (Glück).

The functions of the affected limbs suffer in consequence of the disease ; their mobility is obstructed, and to a greater degree when ulcerations occur.

The *face*, in consequence of the formation of nodules, assumes a typical appearance. The forehead becomes prominent and thickened by a series of closely set nodules interrupted by furrows. The cheeks

PLATE III.

Fig. 28.
(1 and 3) Hindoo girls, (2) Hindoo woman with NODULAR LEPROSY.
(The photograph was kindly given to the author by Prof. Sticker, Giessen.)
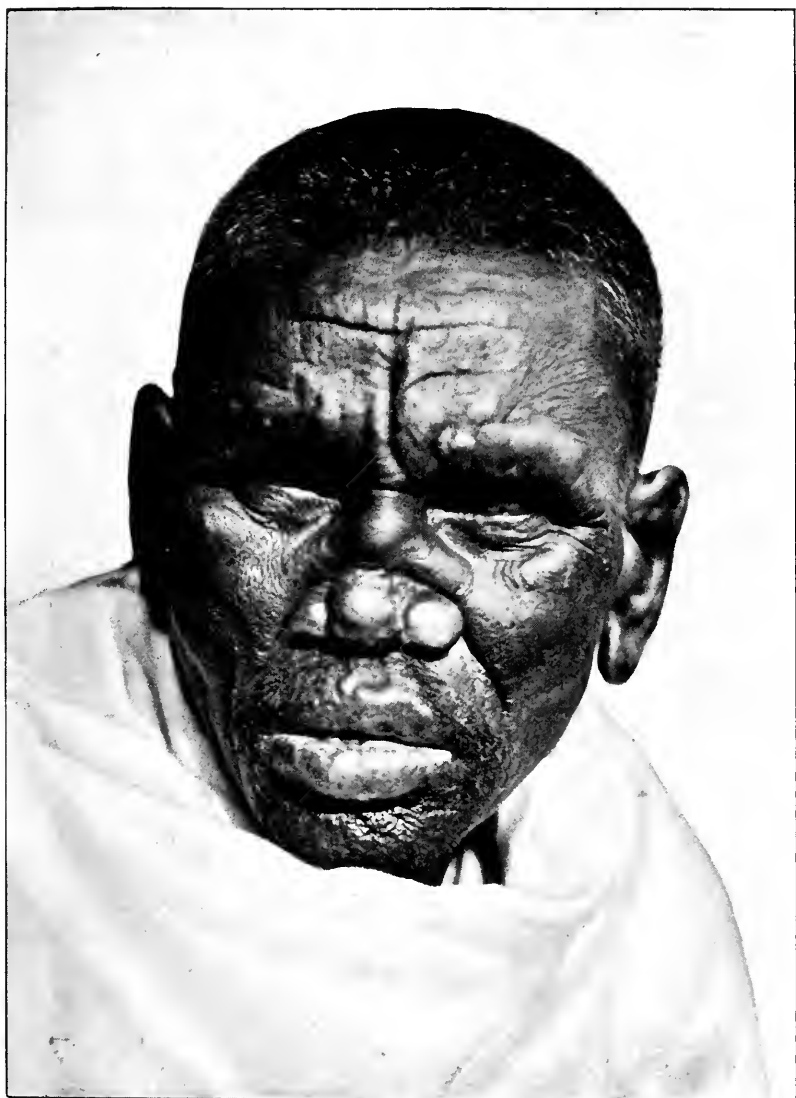
A LEPER'S HEAD,
Showing markedly the loss of Nasal Cartilages.

By kind permission of the Proprietors of " The Journal of Tropical Medicine."

as well as the lips and chin are likewise thickened and beset by nodules of various sizes. The nose appears flattened and spread by the formation of nodules, and the lobes of the ears are thickened and nodular. The hairs of the eyebrows and beard fall off, and the face, in consequence of loss of play of feature, has a stupid, expressionless appearance. In addition, the patients appear older than they really are. The ancients appropriately designated the physiognomy of such patients "Satyriasis," on account of the faun-like countenance disfigured by the nodular formations, and "Leontiasis," because the lepers have a lion-like face caused by the nodules covering it.

The face and the backs of the hands are the places where the nodules mostly first appear. Swelling of the superciliary region and the falling out of the hairs of the eyebrows is one of the first and surest signs of leprosy; however, the lack of these symptoms does not, as has been asserted, exclude the diagnosis of the disease. Unna points out that in pure skin leprosy normal eyebrows are often observed.

The same changes met with on the skin are often proceeding contemporaneously on the *mucous membranes also*, or may set in later. Nodules and infiltrations form in the nose and mouth, on the palate, in the pharynx and larynx, and in the œsophagus. The nostrils, in consequence, become constricted and imperforate, but the senses of smell and taste are maintained a long time in spite of the great nasal and pharyngeal changes (Leloir, Glück).

The voice becomes coarse, hoarse, and tuneless (vox rauca leprosa), respiration becomes retarded, masticatory movements hindered, swallowing difficult, the natural means of taking food may even become impossible, and suffocation may occur. The nodules appearing on the mucous membranes are distinguished by their great tendency to form ulcerations, which, when the infiltrations strike deeper into the tissues, cartilages, &c. situated below, may lead to extensive destruction, such as sinking in of the nose, disintegration of the pharynx, &c. The cicatrisation of the ulcers and shrinking of the scars may also cause intense disfigurements.

Disease of the mucous membrane of the nose is one of the earliest and most frequent symptoms. Sticker, as already mentioned, is of opinion that the primary affection of leprosy is situated in the nose, from whence the disease spreads further in the nose, mostly in the form of an ulcer, over the cartilaginous part of the septum. Instead of becoming disintegrated and ulcerated, the infiltrations of the nasal mucous membrane may also go on to atrophy; the mucous membrane in that case becomes pale, dry, and of a whitish colour, and even the turbinated bones may atrophy. A variety of forms are described by Glück according to the appearance of the nose.

(1) The *flat, hook-nose*—broad, mostly pushed to one side--the tip lengthened and bent more or less against the upper lip.

(2) The *negro nose*—the bridge becoming sunken, the thickened point raised, deep furrows form between the tip and the deeper and thickened alæ nasi; the nostrils, from the front, are turned up, reminding one of the syphilitic nose (Operngucker, Fournier).

(3) The *snout-like nose*.—The bridge and tip are in this case involved by nodules, while the infiltration of the ala nasi is less severe, the nose in consequence being apparently narrower, and the tip longer and thicker.

Josef observed a case of nodular leprosy, not very advanced, with extreme cicatrised *stricture of the rectum*, which he considered of leprous origin. This phenomenon has never been observed by any one else, and the origin of the cicatrices may be otherwise explained.

The *eyes* are also attacked by the disease. Nodular infiltrations very frequently form in the eyelids and may, in rare cases, ulcerate, and after cicatrisation lead to ectropion, entropion, blepharophimosis, trichiasis or

distichiasis. Reddish-grey tubercles, of the size of the head of a pin, appear on the conjunctiva in the vicinity of the margin of the cornea and grow steadily. According to Jeanselme and Morax they almost always originate in the episclera, they only cause slight infection of the conjunctiva in their immediate vicinity, and are unaccompanied by general conjunctivitis or increase of secretion. The small tubercles spread, become confluent or hypertrophied around the *cornea* and finally attack it. The cornea may, however, also be primarily affected by tubercles which are situated nearer to the edge than the middle. They appear as prominent greyish-white spots, each of which is surrounded by a very thick opacity which, however, thins out towards the margins (*pannus leprosus*). The tubercles and opacity may gradually extend to the entire cornea and thus cause complete blindness. Besides this tubercular form of disease, an opacity of the cornea caused by diffuse infiltration may also occur; it starts from the edge of the cornea, gradually spreads over a larger or smaller circumference of the cornea, but generally leaves its centre free. Sometimes also superficial erosions and, in rare cases, keratitis punctata, come under observation. As in the cornea, so nodules and diffuse infiltrations are also observed in the *iris;* the nodules sometimes resemble small miliary tubercles, or in some cases are large as to remind one of gummata ; these may exist in combination with opacity of the vitreous humour in consequence of iridochoroiditis or iridocyclitis.

The *lymphatic glands* appertaining to the parts of the body attacked, participate in the disease and become intensely swollen ; this is most frequently observed in the submaxillary, cervical and groin-glands. The disease has, almost always, a chronic, progressive course, the process of forming tubercles, infiltrations, ulcerations, &c., extending over years or tens of years. Temporary improvements may, indeed, occur and occasionally persist for years, leading one to suppose that complete recovery is not far distant ; but subsequently the disease always recurs.

During the course of the disease atrophy of the testicles sets in, and in consequence the generative capacity of the patient gradually decreases and finally is completely lost ; frequently this takes place in relatively early stages of the disease. In women the menstruation at first becomes irregular and subsequently stops entirely.

Should the disease set in prior to puberty, the physical development of the patients, particularly that of the genitals, is much retarded. The testicles do not become larger than a cherry, the penis remains small, the pubic hairs and the beard are scanty or entirely absent. In girls, menstruation appears late and is irregular, and in the case of leprous children it seldom appears at all (Jeanselme).

The mental powers of patients are not usually affected.

During the course of the disease *attacks of fever* often occur. The prodromal fevers and those induced by erysipelas have already been mentioned above. Moreover, every severe outbreak of nodules, even without prior erysipelas, may be accompanied by fever. Absorption of softened nodules and nodular formation in internal organs also cause fever, which is mostly intermittent, more rarely remittent or irregular. The frequency of the fever seems to differ in the different centres of leprosy. In Japan, according to my experience, the prodromal fever is often lacking, and I also observed fever but seldom during the course of the disease, and then, as a rule, it was but slight. The attacks of fever contribute greatly to still further weakening the patients already sufficiently enfeebled by their disease.

The temperature falls in the cachectic condition and the patients continually complain of feeling cold.

The disease is almost always incurable. *Death* ensues finally, either from exhaustion, or from complications with other diseases that are directly or indirectly connected with leprosy. The most frequent of these are chronic diarrhœa, erysipelas, pyæmic conditions, pulmonary and renal diseases, and amyloid degenerations ; the last named, according to Havelburg, occurring in patients who have suffered loss of strength from the discharge of pus, &c.

According to statistics compiled by Hillis as to the causes of death, the direct consequences of leprosy are responsible for 38 per cent., nephritis causes 22·5 per cent. of the deaths ; lung-diseases, including phthisis, 17 per cent. ; and diarrhœa is responsible for 10 per cent. of the deaths.

As recent investigations have proved, the so-called pulmonary phthisis of lepers is frequently caused by *leproid neoplasms in the lungs ;* and the diarrhœa, of which mention will be made below (see Pathological Anatomy), may be induced by specific disease of the intestine. *Pulmonary phthisis,* according to Danielssen, is especially liable to be set up when the nodules begin to disappear through softening and absorption ; the deposit of nodules in the skin having in the meantime completely withered.

2. Nerve Leprosy.

(Lepra nervorum, anæsthetica, maculo-anæsthetica, glabra, non tuberculata, mutilans, antonina, mal de San Antonio [Columbia, Mexico]).

(See fig. 29, table IV.)

In nerve leprosy, as in nodular leprosy, the actual outbreak of the disease is preceded by *prodromal symptoms*, which, besides *attacks of fever*, are principally of a *nervous* character. Rheumatic or neuralgic *pains* (dull, darting, or piercing), occur in paroxysms in various parts of the body and may be combined with paræsthesia (formication, tingling, numbness, a sensation of heat, itching) ; the members thus affected frequently swelling and becoming red and hyperæsthetic. *Hyperæsthesia*, sometimes local, sometimes more extensive, may set in ; occasionally every part of the body is painful on touch and movement. Hyperæsthesia of the organs of sense (pains in the eyes and photophobia, and also sensitiveness to noise) may appertain to the prodromal symptoms. Danielssen, as also Hansen and Looft, mention the occurrence of slight *vasomotor disturbances* which are exhibited in bluish-red, reticular designs or pale spots, which appear most markedly at changes of the temperature, or may be induced by friction. As an initial symptom, I personally have observed periodical *flushing of the face* and *twitching of the facial muscles*, accompanied by swelling of the features.

Subsequent to these preliminary symptoms, pale red or dark red *spots*, partly flat and partly raised, and of various shapes, develop insidiously as a rule on the skin without fever or deterioration of the general condition. At first small, of the size of the smaller coins, they gradually grow, enlarging from their periphery, while the centre again becomes pale and flattened ; they may become confluent, resembling maps, and in this manner involve considerable areas of the surface of the body. Their edges are either sharply outlined or obliterated, their surface shiny, smooth, or especially at their edges, rough and exfoliatory, so that sometimes the diseased surfaces have the appearance of being powdered with flour (Brieger).

The spots may appear on various parts, sometimes on the face, some-times on the neck, on the trunk, or on the limbs. I have also occasionally observed such spots on the hairy parts of the head. I have never been able to confirm the symmetrical arrangements of either macules or nodules insisted on by some authors. Occasionally the spots cause the patients slight pains, a sense of heat, tension or slight itching. Although they may vanish from isolated spots, they persist at other places and the primary hyperæsthesia gradually changes to anæsthesia.

During the further course of the disease the spots became darker and assume an ashen-grey, sepia-brown or blackish-brown colour (*Lepra nigra*) ; such spots may also appear primarily. The pigmentation is not always even, the centre of the spot being sometimes lighter and sometimes darker. The edges are occasionally sharply defined and sometimes obliterated. These dark spots may in the course of years disappear if the illness has not as yet made further inroads ; whilst in other instances the anæsthesia persists, and the patches become transformed into unpig-mented spots that occasionally are quite white (*Lepra alba*). The white spots may also develop primarily from normal skin.

The appearance of blisters, varying in size from that of lentils to that of the palm of the hand and containing light yellow limpid fluid, is a further symptom which is more especially observed in the initial stage of the disease. The blisters most frequently make their appearance on the limbs, especially on the knees, elbows, the backs of the hands and the dorsa of the feet. In three cases Leloir observed them on the mucous membranes. Mostly one blister only forms, more rarely several appear simultaneously. Occasionally they are induced in consequence of burns or other traumatic influences, often, however, without any such cause. Frequently they set in with remarkable rapidity and persist for several hours or days. After having burst there is an excoriation which is at first red and shiny, and later exhibits a thin whitish-yellow coating, and when healed sometimes leaves either a dark pigmented, or white unpigmented spot ; generally, however, there remains an anæsthetic spot, surrounded by a thin, sepia-coloured border. In consequence of marginal inflammation deeper ulcerations may result from the blisters. The formation of blisters may be repeated at intervals, often for years. They are designated *pemphigus leprosus*, on account of their similarity to pemphigus blisters.

Independently of the spots described above, and occasionally even before their appearance, there sets in a gradual decrease of sensibility, first on circumscribed spaces of skin and later on to a great extent over the body, gradually ending in complete extinction of feeling. This anæsthesia, however, does not occur in the entire region of the ramifications of certain nerves, for a few spots only in the region of the distribution of the nerve may be anæsthetic. The anæsthesia generally starts at the periphery and thence gradually works towards the centre, so that finally the entire limbs and often also parts of the trunk are without feeling. The face also becomes more or less anæsthetic.

As to the various *sensory qualities*, they may be almost equally attacked ; more frequently, particularly at the commencement of the disease, the sensations of pain and temperature are principally disturbed (*dissociation of sensibility*). Occasionally also partial paralyses of sensation occur which affect the senses of touch, pain, locality and temperature in the most manifold combinations. Retardation of the conduction of sensation has also been observed (Neisser). On the touch of a warm or cold object on insensitive parts, the patient at first only becomes aware

PLATE IV.

Fig. 29.

(*a*) Hindoo with NERVE LEPROSY.   (*b*) Hindoo boy with MIXED FORM.
(The photograph was kindly given to the author by Prof. Sticker, Giessen.)

of the contact, but after from five to eight seconds he feels a slight sensation of temperature ; the more the disturbed sensibility the slower the perception ensues. Often there is perversion of sensation ; instead of cold, heat is felt, or a simple prick causes a relatively long sensation. Frequently the delay inducing sensation is very pronounced, only after repeated stimuli at the same place sensation is at last elicited (Jeanselme). The muscular sense and the appreciation of the position and placing of the limbs always remains intact. After the skin, the less superficial parts down to the bone may be attacked by paralysis of sensation.

Jeanselme states that during the period of anæsthesia recrudescences of hyperæsthesia often set in at irregular intervals ; these generally occasion an aggravation of the sensory disturbances, but sometimes after them sensation returns to places previously without feeling.

As to the condition of the *tendon reflexes*, the statements of authors do not coincide. According to Goldschmidt, they are already diminished at the commencement of the disease, and later on disappear entirely. Bälz found them remarkably increased and only absent when the nerves were entirely destroyed. Of 24 cases observed by Jeanselme, 4 exhibited normal knee-jerk, 6 diminished or extinguished knee-jerks and 14 increased patellar tendon reflexes. According to A v. Bergmann the reflexes are not essentially altered.

The *nerves* appertaining to the parts of the body attacked are often *thickened* and present either knotty or spindle shape enlargements. This, according to my experience, is most frequently observed in the great auricular nerve and ulnar nerves, more rarely in the peroneal and more seldom still in the radial, median and supra-clavicular nerves. According to Bälz the great auricular nerve is of particular importance for diagnosis, as he found it thickened in 90 per cent. of all cases. In rare cases he also observed thickening of the facial and supraorbital nerves. The most extensive indurations occur in the ulnar nerve, the diameter of which above the elbow joint is occasionally greatly increased. At the commencement of the disease the nerves are exceedingly sensitive to pressure, which induces neuralgia and paræsthesia in them, or increases the pain extant. As the disease advances the sensitiveness of the nerves gradually disappears.

Motor disturbances are introduced with the alterations in sensation, but not to the same extent, for with them it is not the question of actual paralyses but of *atrophy of the muscles*, and in consequence the decrease of muscular power. The decrease of muscular power is generally on a par with the diminution of the size of the muscles. The disturbance most frequently affects the face, the hands, and the feet ; the muscles, however, are not apt to be attacked to an equal degree, for of muscles governed by the same nerves and quite close to each other some may be affected and some remain free.

The *muscles of the face* are atrophied and paralysed to a variable extent and intensity ; the face in consequence loses all expression, and has a vacant, stupid appearance, which is still further increased by periodical twitchings of the facial muscles, which impart the impression of idiotic grins. In rare cases the masseters become so atrophied that the lower jaw drops and has to be maintained in its natural position by a bandage (Hansen and Looft). In consequence of the atrophy of the orbicular oris muscle, the lower lip falls away, the mouth can only be closed with difficulty, and the saliva dribbles. Through the atrophy of the orbicularis palpebrarum it becomes impossible to close the eyes, and paralytic lagophthalmos and ectropion of the lower eyelids ensue. Thereby the lower

punctum lachrymale is separated from the eyeball, causing the tears to flow down over the cheeks, and this imparts a still more pitiful expression to the countenance. The muscles of the eyes also may be attacked separately (strabismus, diplegia), or together (ophthalmoplegia) (Jean-selme).

In consequence of the defective closing of the eyelids the eyes suffer; and more particularly is this the case if the anæsthesia of the conjunctiva and cornea are induced by disease of the trigeminal nerve. Ulceration of the cornea frequently results, and may lead to perforation or staphyloma, and finally to atrophy of the globe; or xerophthalmos with a condition of the cornea resembling mother-of-pearl may develop.

In a series of cases, v. Düring and Trantas, as also Bistis, observed black, white, and mixed spots of various shapes in the choroid, more especially in the peripheral parts.

Motor feebleness is perceptible in the *hands :* the patient cannot hold on tightly and drops light articles. Tremor of the hands is also observed. The muscles become attenuated, and this is particularly perceptible in the thenar and hypothenar eminences and also in the interossei muscles. In consequence of the preponderance of the flexors the fingers are curved inwards to the palm, the first phalanges being extended (*claw-like hand, main en griffe*). Connected with the claw-like hand there may be a deviation of the four fingers to the ulnar side, caused probably by acute attacks of pseudo-rheumatism (see below). Contractions of the fingers, particularly the fourth and fifth, are not rare, and according to my observations, belong to the earliest symptoms of disease, even preceding the appearance of anæsthesia, muscular atrophy, paralysis and cutaneous eruptions.

Moreover the *arms* and *legs* are attacked, and their movements, in consequence, hampered. The muscular system of the ulnar side of the forearm is the first to become atrophied, the radial aspect is only affected much later; the muscles of the legs become atrophied at a later period still, and to a much less degree. The toes may become contracted as well as the fingers, but this is of rarer occurrence; to a slight degree also the arms and legs may also be contracted. I have never observed complete paralysis of the limbs; as a rule, the patients are able to walk and move their hands.

The *electrical excitability* of the atrophied, paralysed muscles diminishes, the indirect even more than the direct (Bidenkap and Leegaard), and in a few muscles, as F. Schultze first pointed out, a complete partial reaction of degeneration occurs.

Increased *mechanical excitability* and *fibrillar twitchings* are, moreover, occasionally observed in the affected muscles. According to my observations, on the other hand, neither ataxia nor staggering with closed eyes occurs in leprosy in spite of the severe and extensive anæsthesia.

Disturbances of a *trophic* character accompany the sensory and motor disturbances in the affected parts of the body. The skin becomes thin, dry, rough, lustreless, exfoliated, wrinkled, and is frequently removable in large flakes, or it may on the contrary be smooth and shiny on the fingers and toes and without folds (glossy skin). Œdema frequently appears in the legs and hands. Habel observed blue œdema on the hands and feet, which were swollen and of a livid blue colour. An elephantoid hyperplasia occasionally forms under the influence of the œdema, in some cases only affecting the toes, and in other cases extending to the

middle of the leg. Hansen and Looft also frequently observed darkly tinted and usually symmetrical hyperkeratoses on the anterior aspect of the legs and on the backs of the hands.

Bälz recommends the inunction of aniline dye for the recognition of leprous spots : the part of the body in question is rubbed with fuchsine or methylene violet powder, lightly covered with absorbent wadding and then 0·01 to 0·02 pilocarpin is injected subcutaneously. The healthy parts perspire freely, the powder dissolves, and the well-known colour from the respective dyes appears. The leprous spots do not perspire, and therefore are sharply defined against the healthy parts. This method succeeds in rendering apparent leprous regions which are otherwise hardly perceptible.

The *hair* becomes dry and brittle and falls off; according to my experience the dropping out of the hair of the eyebrows is frequently one of the earliest symptoms of the disease.

The *nails* lose their normal gloss, become diagonally and longitudinally grooved and rough, and are transformed into brownish, discoloured, thick, misshapen brittle masses, or they wither, become thin and fall out entirely.

The *tendency to ulceration* is another consequence of the disturbed nerve-functions appearing in the later stages of the disease, and caused partly by the anæsthesia and partly by trophic disorders. The ulcerations are frequently originated by trifling injuries, and are particularly liable to be set up on the extensor aspect of the fingers and hands, and on the soles of the feet. The ulcers are mostly indolent, and as they have but little tendency to granulate they persist for months and years. They have hard callous borders and a completely atonic base which secretes a scanty opaque viscid fluid. On the soles of the feet the ulcerations frequently appear as perforating ulcers; they are round and have a sharp border, appearing as if cut out with a punch. In other cases they assume the form of fissures and rhagades with hard callous edges and smooth pale red bases, which run obliquely in the flexor folds of the fingers and palms of the hand.

The ulcers grow deeper and may lead, through disintegration of the joints, to the casting off of single phalanges of the fingers and toes, or to the removal of entire fingers and toes. More extensive mutilations, such as the loss of an entire hand or foot, are said to occur; this is, however, a very rare result, nor did I ever see a case of this sort amongst the numerous lepers that I had the opportunity to observe in Japan, China, Siam, Java and Ceylon. Frequently it is not the third or terminal phalanx that is cast off, but the first or second, so that after cicatrisation of the ulcer the ungual phalanx may be situated upon the first phalanx, or upon the metacarpus or metatarsus.

Mutilations of this kind may originate in a different manner. The process may have its origin in the *bones;* according to A. v. Bergmann and Geill this is the case as a rule. The phalanges become necrotic and are then cast off through suppuration, the surrounding soft parts then retracting.

In yet other cases the mutilation is caused by simple *absorption of the tissues.* Bälz describes this process, which he regards as the usual cause of the mutilations, as follows : First, the central piece of the first phalanx softens, the lime salts disappear, and a sort of pseudo-arthrosis ensues, the articular ends of the phalanx approach one another, and gradually experience the same fate, the finger becoming then shorter by a joint. In the meantime, or somewhat later, the same process begins in the second phalanx, and finally in the distal phalanx, the upper end of which, bearing the nail, resists longest. The soft parts covering the bone become

shortened simultaneously with the bone. The nail also gradually disappears, and the appearance is exactly as if the finger had been amputated without a cicatrix being present. Kalindero and Miura traced the process with the assistance of the Roentgen Rays.

A kind of *dry gangrene* may also lead to the shedding of fingers and toes.

In rare cases the loss of fingers and toes is effected by means of an *ainhum-like process* (see ainhum). Ehlers, in three cases, observed ainhum-like grooves at the toes.

Nerve leprosy is also entitled *Lepra mutilans*, on account of the mutilations to the limbs that take place in the course of the disease.

A sort of osteo-malacia has also to be mentioned amongst the trophic disturbances. The members attacked by it assume eccentric forms which Danielssen and Boeck compare to the fin of a seal (Jeanselme). *Crippled and atrophied conditions of the feet* are also observed corresponding with Charcot's "*pied tabétique*" (Heiberg). Hansen and Looft, moreover, mention the occurrence of *acute rheumatoid articular affections* accompanied by effusion in the earlier stages of the disease. They generally affect the small joints of the fingers and hands, and also the articulations, the knees and feet; they mostly appear simultaneously with a macular eruption, disappear again, may be repeated, and finally may lead to thickening of the joints and ligaments, and to stiffness.

Gastralgia was observed by Danielssen and Leloir, and the latter compares it to the gastric crises of tabetics.

Sexual functions, as in the nodular form, gradually decrease in both sexes and finally cease altogether.

The patients become feebler and feebler, their bodily temperature sinks and the action of the heart is impaired.

In far advanced cases of the disease, according to the investigations of Winiarski, the hæmoglobin and the number of red corpuscles, which at first were not essentially changed, diminish considerably in the nodular as well as in the anæsthetic form. The white blood corpuscles generally remain normal, the poly-nucleated forms predominate considerably; the fibrin is increased, according to Rake in 50 cases it amounted on an average to 0·76 per cent. (according to Becquerel and Rodier, 0·22 per cent. is the normal quantity).

Brieger and Elsner in one case of nodular leprosy, found the acid ethyl sulphates ot the urine considerably increased, and the proportion of the sulphuric acid of the salts to the ethyl of the sulphate as 2·1 (average number = 10·9). This condition appertains to the diseases, designated by Brieger, *septic diseases*, such as diphtheria, scarlet fever, erysipelas, pyæmia, in which, in consequence of abnormal putrid decomposition, a larger quantity of putrefactive products are formed than in other infectious diseases.

The intelligence of the patients is maintained intact for a long time, but there is a mental and moral obtuseness about them. As Corre strikingly expresses it: " C'est avec une sorte de stoïcisme indifférent que le malheureux lépreux assiste chaque jour à la destruction de son être."

The patients finally, as in the nodular form, succumb to general exhaustion, or death occurs through diseases directly or indirectly connected with leprosy. Not infrequently they die in fits of coma or delirium accompanied by high temperatures, a condition which occurs more frequently in this form than in nodular leprosy.

The course of the disease as already mentioned is, as rule, a very slow one in both forms, but in nerve leprosy it is even much slower than in nodular leprosy. The duration of the disease in Norway is computed as eighteen or nineteen years for nerve leprosy, and eight or ten years (Danielssen and Boeck, Bidenkap) for nodular leprosy. In the Baltic provinces the duration is respectively eighteen years, and nine or ten

years (Hellat). In the British Colonies fifteen to twenty years, and nine to twelve years respectively ; these figures tally well with each other. Impey gives a shorter average duration, namely, five years five months for the nodular form, eleven years five months for the anæsthetic form, and nine years three months for the mixed forms, these figures being the result of his experience on Robben Island, off Cape Town. In the district of Memel, according to R. Koch, five to ten years is the period for the nodular form. On the Sandwich Islands, where likewise the nodular form preponderates, the disease, according to Hillebrand, only lasts from three to five years. It must, however, be remembered that the duration of the disease is essentially influenced by certain circumstances, the care bestowed on the patients and their manner of living, and also the appearance of intercurrent diseases that may cause a speedy death. Under some circumstances the duration of the disease may be remarkably long, as proved in the case (mentioned by Lima) of an African negro who died in the leper asylum at Rio de Janeiro, after a stay there of sixty-five years.

In most leprous countries the anæsthetic form is the more frequent ; but in a few places, such as Norway (Memel) Spain, Portugal, Madeira, Trinidad, Brazil and in the Sandwich Islands, the nodular form is the more prevalent.

It has been asserted that the form of the disease depends on *climatic influences* (moisture, temperature). In Norway, according to Hansen and Looft, the nodular form is more frequent in regions with a damp climate, and the anæsthetic form in places with a dry climate. Japan, however, for instance, has a very damp climate, yet according to my observations, the anæsthetic form preponderates. According to Impey and Ehlers, the nodular form is more frequent in cold climates and the anæsthetic form prevails in hot and temperate climates. Nevertheless, the nodular form preponderates in tropical Brazil and in the tropical Sandwich Islands.

According to my opinion the length of the endemicity plays an important part. In countries in which leprosy is only of recent date the nodular form preponderates, while on the contrary nerve leprosy prevails in places where the disease is old and deep-rooted. Thus in the district of Memel (Norway) and in the Sandwich Islands (where leprosy was imported about the middle of last century), the nodular form prevails almost exclusively, or at any rate by far more frequently than the anæsthetic form, whereas in the Asiatic countries, such as China and Japan, where the disease has been endemic probably for thousands of years, nerve leprosy prevails. The anæsthetic is the milder of the two forms—longer duration, less number of bacilli, slighter contagiousness, greater tendency to cure in that sense in which cure can be spoken of in leprosy. In countries where the disease has been endemic for ages, and in consequence the population are inured to it and possess greater immunity, the milder form occurs ; whereas in countries where the disease is of more recent date the severer form prevails.

Besides the well-marked forms, cases occur in which there are only one or two symptoms of leprosy, mostly confined to one limb ; for instance, circumscribed anæsthesia on the forearm, particularly in the ulnar region, with contraction of one or two fingers ; anæsthesia and muscular atrophy of forearm and hand ; isolated maculæ with anæsthesia ; one or two mutilated fingers. According to the best of my knowledge I was the first to describe these and designated them *local leprosy*. Arning, later, called them *abortive leprosy*. In the case of one of my patients, blisters formed on the right knee several times a year ; these changed into ulceration, which on healing left anæsthestic places, so that gradually the entire knee and its vicinity had become anæsthetic. The patient besides had lost the hairs from his eyebrows, but there was a complete absence of all other symptoms of leprosy, although the disease had already persisted for eighteen years. Besides Arning and myself, Zambaco, Morrow, Coffin, Ehlers, A. v. Bergmann and Crespin have described cases of this kind.

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There occurs in the Pyrenees, especially in the district of Béarn, a disease that is there well known. It consists of deformity of the nails and finger tips, with the subsequent loss of the last phalanx, and alopæcia. The disease is regarded as a form of leprosy gradually weakened by inheritance (Magitot, Regnault, Layard and others). The sufferers are called *Cagots*, a word Magitot considers corresponds with *Cacou*, the Celto-Bretonic term for lepers.

Occasionally *complications* of leprosy with other *skin diseases*, such as syphilis (in Norway this mixed form is called *radesyge*), elephantiasis, arabum, eczema, psoriasis, favus, &c., occur. The complication with *scabies* is the most interesting. Horny, dry scabs, often several centimetres thick, form on the extremities and other parts of the body, the scabs project like the bark on the tree, and under them living and dead itch insects in great numbers are found ; these scabs are allowed gradually to develop unmolested because the sensation of itching originated by the acarus is not felt in consequence of the anæsthesia of the skin, and therefore the action of the acarus goes on unchecked (*scabies norvegica* or *crustosa*).

PATHOLOGICAL ANATOMY.

In the *nodular form* circumscribed *nodules* or *diffuse infiltrations* are found in the skin and mucous membranes. The nodules consist of a jelly-like, yellowish-white to reddish-black substance permeated by a voluminous vascular network. On section this substance exhibits a smooth glossy surface, and on pressure a viscid slimy fluid exudes. Parts distinguished by a brown colour are sometimes seen.

The leproid neoplasms are of the nature of *granulomatous excrescences* and are therefore histologically related to the syphilitic and lupoid nodular growths. Under the microscope it will be seen that they are composed of scanty fibrillar interstitial tissue, and of cells of various kinds, particularly of the small round type about the size of leucocytes, of epitheloid fusiform cells, and of the so-called *leprosy cells* which Virchow first described. These are large, round, or oval cells, with several nuclei and vacuoles which have already been mentioned (p. 235). From these *giant* cells, with twelve or more nuclei at their periphery, may develop. A great many of the cells contain the bacilli described above, some only a few, others, especially the leprosy cells, are literally crammed with them. In the upper strata of the neoplasms—increasing in number according to the age of the latter—there are to be found besides, peculiar large round heaps, the *globi* already alluded to, and it is to these that the leproma owe their brown colour. According to the investigations of Thoma, Rikli, Unna, Baumgarten, Schäffer and others, Langhans' giant cells also are present in the leproma.

The leprous neoplasms are rich in vessels, in the vicinity of which there are agglomerations of cells. These are generally grouped round the adventitia of the blood vessels (lymph spaces). In the skin the neoplasms advance towards the surface and infringe upon the epidermis, from which, however, they are always separated by a free sub-epidermic zone ; downwards they force their way deep into the subcutaneous adipose tissue. The neighbouring tissues (hair follicles and glands) are displaced by the neoplasms and partially atrophied.

The nodules and infiltrations often remain stationary for years. Their occasional softening and ulceration can mostly be traced to external causes. Necrosis and caseation may, according to the investigations of

Babes and others, occur in the nodules. More frequently, however, absorption occurs, leaving behind either brown pigmented or unpigmented patches, with somewhat thickened skin.

The *maculæ* of the anæsthetic form are, at least in most cases, induced by the same neoplasms ; they therefore are but slighter diffuse infiltrations, differentiated, however, from the nodules, by far more scanty bacillar contents, by the lack of the large bacillary formations (leprosy cells, globi) and by a tendency to be transformed into connective tissue, thus inducing a decay of the bacilli and serving to explain the reason that bacilli are rarely found in old spots. White spots may also result in trophic disturbances through affections of the nerves.

Unna regards the maculæ as neurotic inflammations caused indirectly by the bacilli invading the nerves of the skin ; he differentiates them as *neuroleprides* from the *lepromata* which are caused by the presence of the bacilli in the skin itself.

In other particulars *nerve leprosy* is a disease of the nerves in which, and in the interstitial connective tissue of which (peri-, epi-, and endoneurium), the same proliferations develop as in the skin and mucous membranes and lead to their thickening (perineuritis leprosa, Virchow). The indurations are sometimes diffuse and sometimes fusiform, and appear particularly at places where the nerves run superficially over bones and joints, and where they are exposed to pressure and extension, as in the median at the wrist joint, in the ulnar at the elbow and in the peroneal where it crosses the fibula (Hansen and Looft). These nerves frequently exhibit a greyish or brownish colour. According to Dehio the thickening always becomes more considerable towards the peripheral end, decreasing towards the centre, the process of disease seemingly starting at the periphery and gradually creeping up the nerves. The bacilli in the nerves compared with those in the nodules are few, and in the maculæ the great bacilli-containing formations are absent.

According to Dehio, one may observe microscopically a small-celled infiltration, consisting of leproid neoplasms round the nutrient vessels of the nerves. The nerves themselves as they pass through these neoplasmic growths appear but little diseased or quite healthy to the naked eye. In parts where the disease is further advanced the neoplasm may be seen to spread to the connective tissue isolating the separate bundles of nerves, so that the trunk appears distinctly thickened. At this stage there need be as yet no loss of nerve substance ; but in course of time one may observe how in the peripheral parts the leprous tissue has forced itself between the single nerve fibres, causing them to become atrophied. Next to nerve-fibres that are still normal, one finds in other nerves that the medullary sheath is more or less disintegrated or quite lost, so that only the axis cylinder remains intact. At last this also is destroyed and in its place a small tube-like gap is left that finally also disappears. In the last stages of the disease all the nervous elements are destroyed and, instead of the original nerve-trunk or nerve-branches, there is a thick cord in which only the perineurium and connective tissue nerve sheath are left. Finally, the newly formed tissue may become purely cicatricial tissue, and the nerve that was previously thickened may in consequence shrivel and become thinner than normal, in which case scarcely anything but connective tissue can be found on microscopic examination (Hansen and Looft).

Dehio and Gerlach, on the basis of a case observed clinically and minutely examined anatomically, have come to the conclusion that in the anæsthetic form also the disease commences in the skin. The local circumscribed anæsthesias caused by the flat leprous neoplasm spreading in the diseased skin, invade the lymph spaces and lymphatics in the skin and penetrate the tubular tissue spaces in which the most delicate terminal branches of the skin nerves are distributed. In consequence the skin nerves within the maculæ are disintegrated, and the maculæ become anæsthetic. In the further course of the disease the neoplasms proceed upwards by way of the nerve sheaths, creeping gradually to the larger ramifications and finally to the nerve-trunks. No leprous infiltrations were found in the muscular branches, but only a degenerative atrophy of the nerve-fibres, which was undoubtedly progressing downwards. Still, every leproid disease of the nerves is not ascending, as was proved by the case of nodular

leprosy examined by Nonne, and in which the swellings of the nerve trunks exhibited extensive changes while their periphery and their muscular branches and skin nerves exhibited no changes worth mentioning.

The *atrophied muscles* exhibit microscopically simple atrophy of the muscular fibres with an increase of the nuclei, and of the interstitial connective tissue with interstitial deposit of fat. In very marked atrophy, the muscular fibres completely disappear, and only connective tissue and fat are found. The muscular atrophy is secondary and is caused by the disease of the nerve endings (Hansen).

The degenerative atrophy of the nerve fibres, which is a *consequence of the leprous proliferations* in the interstitial connective tissue of the nerves, explains the disturbances of sensation, the hyperæsthesia, the neuralgia, the anæsthesia, the muscular atrophy with the characteristic changes of the electrical excitability, and the contractions. The phenomenon of anæsthetic and sensitive areas in the same nerve region, as well as of atrophic next to intact muscles, is explained by the fact that all nerve fibres in a nerve are not symmetrically destroyed, a part of the nerve remaining unaffected. In contradistinction to other diseases of the peripheral nerves (polyneuritis, beri-beri), the sensory fibres are, in leprosy, attacked in the first place, the motor disturbances are less than the sensory. In the various trophic disturbances also that characterise the anæsthetic form of leprosy, the atrophy of the skin, the falling out of the hair, the changes in the nails, the appearance of vesicles, the formation of ulcers, the mutilation of the limbs, &c., the explanation is afforded by the nature of the disease of the nerves and the impairment of the trophic fibres.

Formerly leprosy was regarded as a primary disease of the *spinal cord.* It is true that in a series of cases changes were found in the cord, such as hyperæmia (particularly on the posterior aspect), inflammation of the spinal meninges, granulomatous proliferations within the cord (as a continuation from the nerve sheaths with consecutive atrophy), sclerosis, extensive softening of the spinal cord, atrophy of the ganglion cells of the posterior cornu of the spinal cord and of Clarke's columns, degeneration of the lateral and posterior columns (particularly Goll's columns), atrophy of the posterior roots and fibrous degeneration of the spinal ganglia. In many cases, however, the spinal cord was found to be quite normal, so that the above conditions were incidental merely. The changes mentioned are partly to be attributed to secondary lesions, symptoms arising in consequence of the primary disease of the nerves, and are partly attributable to direct injury caused by the invasion of bacilli; partly they are mere incidental complications exercising a variable influence on the symptomatology of the disease.

The same leproid neoplasms that are formed in the skin, mucous membranes and nerves, also occur in the *cornea, cartilage, lymphatic glands and internal organs.*

The *lymphatic glands* in leprosy exhibit a remarkably characteristic appearance, described as follows by Hansen and Looft : "The glands are universally enlarged without alteration in shape. On section, the centre and trabeculæ are observed to be of a yellow or yellowish-brown colour ; this colour imparts so peculiar an appearance to the glands, that it cannot be mistaken for anything else. . . . The glands are permeable, but the passage of lymph is often palpably restricted in consequence of the ducts being dilated. . . . On microscopical examination it is found that the gland tissues are more or less filled with brown bodies or globi. These are unmistakably the lymphatic cells which are filled with bacilli and with their products of disintegration, namely, granules."

In regard to the nature of the *visceral* changes in *leprosy* there is no complete agreement amongst authors ; the reason being that the microscopic differential diagnosis between leprosy and tuberculosis presents great difficulties.

It is generally agreed that lepromata may be present in the *liver, spleen,* and *testicles*

The *liver* is usually much enlarged, becomes more or less hard, and exhibits yellow streaks and dots beneath the capsule and on the incised surface. Microscopically leprous tissue with numerous bacilli are observed, the latter by predilection grouped around the ramifications of the portal vein. Arning, in one case, observed a hepatic abscess the size of a pigeon's egg beneath the peritoneal covering, the walls of which were formed of leprous tissue.

The *spleen* is often enlarged, sometimes to an enormous extent, and, like the liver, permeated by yellow dots and streaks. The localisation of the infiltrations corresponds mostly to the course of the vessels and to the trabeculæ of the spleen.

In the *testicles* and *scrotum* interstitial infiltrations appear, and these conduce to the atrophy of the seminal tubules and gradually lead to a proliferation of connective tissue. Arning and Babes also found leproid infiltrations in the ovaries.

The impotence and sterility that gradually develop in lepers is attributable to these disorders of the sexual organs and tissues.

The occurrence of lepromata in the *lungs* and intestine is disputed by Hansen and Looft, who base their statement on the fact that they have never observed a leprous bronchial or mesenteric gland. On the other hand, Bonome, Doutrelepont, Wolters and Arning are of opinion that pulmonary leprosy exists, and the case observed by Doutrelepont and Wolters, in which the sputum during life contained numerous bacilli lepræ, should place the point beyond dispute. The lungs in this case appeared to be macroscopically healthy with the exception of small lobular areas in the right upper and lower lobes. These microscopically proved to be peri-bronchitic infiltrations of the alveolar septa with numerous cells and globi containing bacilli; the bronchial glands in this case were typically diseased.

As to the *intestine*, Doutrelepont and Wolters in their case found spots under the muscularis mucosa, and Schäffer in one case discovered, close in front of Bauhin's valve, a few somewhat raised whitish-yellow areas with depressed centres which were found to consist of leprous tissue. In this case there was also leproid disease of the mesenteric glands. v. Reisner, in one case in which the lungs were normal, observed ulcerations, which he regards as leprous, in the colon and ileum. The ulcerations were roundish and flat and had sharp indurated edges. The infiltration only extended to the mucosa and sub-mucosa. There were no caseations and giant cells, but there were numerous clumps of bacilli and bacilli lying alone.

Doutrelepont and Wolters, as well as Schäffer, found leprous infiltrations in the *kidneys*, mostly in the vicinity of the vessels. Moreover, *nephritis* of one form or another (acute nephritis, large white kidney, mixed form, atrophied kidney) is often present. Out of 78 *post-mortem* examinations, nephritis was found twenty-three times by Rake. *Amyloid* degeneration is also sometimes observed in the kidneys as well as in the liver and spleen.

A few observers (Philippson, Schäffer) have met with the *simultaneous presence of leprosy and tuberculosis*—leprous tissue rich in bacilli, and sprinkled with tubercles with central caseation and a few bacilli in certain organs, especially the liver, spleen and lungs. As, however, recently caseation has also been confirmed in leprous neoplasms (see above) it is doubtful if in these cases it was a question of mixed infection. To decide this point it would be advisable to avail oneself of experiments on animals, in which case negative results would exclude tuberculosis.

The *vascular system* is affected in the form of periarteritis and endarteritis and phlebitis (phlebitis nodularis, Glück), which may probably lead to partial obliteration of the vessels.

In the *bones*, the following conditions may prevail : osteomyelitis (agglomerations of leprous tissue in the bone marrow and in the cancellous tissue), necrosis, caries, and processes of absorption, which, commencing at the periphery, transform the bone into connective tissue (Miura).

In the anæsthetic form the *joints* are described by Hansen and Looft as undergoing changes such as occur in tabes and other diseases of the spinal cord, with trophic disturbances ; there is thickening and villous proliferation of the synovial membrane, looseness of the capsule, destruction of cartilage and subluxation. Articular affections of a tubercular character are occasionally observed, especially at the tarsal and wrist articulations (Hansen and Looft).

DIAGNOSIS.

It is easy to recognise well marked cases of leprosy in countries where the disease is endemic. On the other hand the diagnosis of undeveloped cases in countries free from leprosy may be difficult. In doubtful cases it is important to discover if the person in question has been staying in leprous countries, or has had personal contact with lepers. There is quite a number of cases in literature—those of Köhler, Beigel, Klemm, Meyer, Langhans, and others—which have been described as cases of spontaneous leprosy originating in regions free from the disease, but which were certainly not such. There are no genuine, scientifically confirmed cases of leprosy in countries free from leprosy (Neisser).

The diagnosis is placed beyond doubt by the *demonstration of the leprous bacillus*. The *nasal secretion* is the most suitable for this purpose (see fig. 27, table I.), in which, according to Sticker's researches, bacilli are found, even in the greatest number of cases of nerve leprosy. Kalindero advises that the fluid of vesicles be examined ; but the vesicles should not be opened for this purpose until the contents have become purulent (three or four days). According to Neisser the demonstration of the bacilli frequently succeeds in the nodular form, but mostly fails in the anæsthetic form. Tschnernogabow advises that the tissue fluid which is abstracted from the diseased skin by means of deeply inserted glass capillaries be used for examination. Martin recommends that the serum which exudes when a nodule is squeezed with a pincette, such as is used for squeezing the vaccine pustules of calves be used for examination. The material for demonstrating bacilli may be obtained by pricking nodules, infiltrations, or nerves, or still better by excising a small piece of either, and pulverising it in physiological muriatic acid.

Under some circumstances leprosy may be confused with :—

Elephantiasis arabum.—In this disease the lower extremities and the genitals are principally affected, becoming swollen and thickened : maculæ and anæsthesia are lacking.

Syphilitic gumma.—In the differential diagnosis the following must be taken into account : the situation of the nodules, which in leprosy transform the face in a typical manner ; the formation of ulcerations, which in leprosy do not attain the dimensions and depth of those of syphilis ; the presence of a skin eruption, which has a very different appearance in the two diseases ; and the occurrence of anæsthesia, which does not exist in syphilis.

Lupus.—In this disease the nodules are smaller and exhibit peripheral advance ; spots and anæsthesia are lacking.

Mycosis fungoides (multiple granulomatous excrescences of the skin).— In this disorder the proliferations do not present the typical facial lesions of leprosy, and maculæ, anæsthesia, &c., are absent.

Albinism and vitiligo.—In these there is no anæsthesia, and other symptoms of disease are wanting.

Molluscum fibrosum.—In this complaint the proliferations vary in size from that of a pea to a fist ; they are usually pedunculated and appear in early childhood ; maculæ, disturbances of sensation, &c., are not extant.

Parasitic sycosis.—In this affection the nodules and pustules are situated round the hair follicles and are confined to the face ; other disturbances are not present.

Scleroderma.—In scleroderma the skin is at first thickened and later on attenuated. There are no nodules and blisters, and anæsthesia is less

marked than in leprosy. Ulcerations certainly do occur, but never lead to mutilation of limbs. Both diseases exhibit maculæ and muscular atrophy.

Syringomyelia and *Morvan's disease.*—The differential diagnosis between these two diseases and leprosy is particularly difficult in some cases. In syringomyelia, in which it is a question of a central disease of certain segments of the spinal cord, namely, the dorso-cervical, the trophic and sensory disturbances (mostly) only affect the arms, whereas leprous muscular atrophy attacks the small muscles of the hand and foot in particular. Syringomyelitic atrophy, on the other hand, begins at the proximal parts of the extremities (the scapulo-humeral type is relatively frequent), and in consequence of the participation of the muscular system of the trunk scoliosis often sets in. As to the anæsthesia : in nerve leprosy it is not confined to certain nervous regions, but in syringomyelia the anæsthesia is fairly strictly confined to the nerves that originate from the diseased parts of the spinal column. Dissociation of sensibility occurs in both diseases. In the leprous skin the secretion of sweat mostly ceases early, whereas in syringomyelia hyperidrosis persists for a long time in those regions of the body that are attacked. In syringomyelia, moreover, there are spastic symptoms in the lower limbs, with paralysis of the bladder and rectum, nystagmus, immobility of the pupil, and dysphagia. On the other hand, maculæ, nodules and infiltrations are absent, as are also thickening of the nerves, glandular swellings and loss of the hairs of the eyebrows.

The symptoms of Morvan's disease essentially consist of ulcerations which develop on atrophic and anæsthetic or analgesic parts of the limbs and lead to mutilations. It will be observed that these symptoms may likewise be present in syringomyelia as well as in leprosy. Zambaco, therefore, certainly goes too far in considering Morvan's disease in every case to be a weakened form of lepra anæsthetica, a remnant of ancient leprosy. Cases, however, occur, though rarely, in which the decision as to the disease having been syringomyelia or leprosy is only settled at the *post-mortem* examination.

PROGNOSIS.

The prognosis of leprosy is very unfavourable, for, according to the unanimous opinion of all thorough leprologists, the disease as a rule is incurable. All reports as to recoveries of separate cases, such as have been brought forward recently, should be accepted with caution. They all are open to the reproach that they were observed for too short a time after the supposed recovery, and too little consideration has been given to the fact that leprosy without any treatment occasionally comes to a standstill for several years, and even a retrogression of the symptoms may occur.

Even to-day Wernich's words may be taken at their full value : " It may be asserted more freely of leprosy than of any other disease that no leper before his death can deem himself free of his affliction. The few reports as to cures of leprosy make no more impression on medical credulity than similar miracles mentioned in the Bible."

Removal from the place of contamination to a non-leprous country has a favourable effect on the progress of the disease, inasmuch as it causes it to be milder and slower. Patients in districts where leprosy does not occur have therefore always more chance of amelioration than patients in leprous countries.

PROPHYLAXIS.

As leprosy is incurable, the principal stress is laid on prevention of this horrible disease. This is accomplished by *avoidance of any contact with lepers*, and this purpose is most successfully attained by *isolating* the sufferers from this disease. Experience has taught us how favourable an influence isolation has in preventing the spread of the disease, so that we may hope by these means to extinguish leprosy in course of time. Humanity naturally prohibits the application of compulsory measures, being reminiscent of the cruel mode of action practised during the middle ages. The chief thing to do is to erect leper asylums and leper colonies of sufficient size and number in the countries where leprosy is endemic. In these, as in every other good hospital, there should be sufficient dwelling space and plenty of clothing, food, nursing, medical treatment and occupation for the patients (agriculture and gardening are suitable occupations) ; their religious and other needs should be studied and a certain degree of freedom of action should be accorded to them, so that they feel they are well treated in such places, and go to them voluntarily. Permission should also be accorded to the patients to bring their families, or at least the husband or wife, as the case may be, into the leper asylum. It is better for the children to be entirely separated from their parents and brought up at the expense of the State or the community. When this is not practicable they should at all events be provided with separate dormitories in the asylums.[1] Isolated islands are particularly adapted for the establishment of leper colonies.

By a shelter such as this the lepers themselves are benefited ; the improvement of the hygienic conditions always has a favourable influence on the course of disease of lepers who mostly live in dirt, misery, and want. In consequence of regular, moderate occupation and suitable and sufficient nourishment, their general condition of health improves. The ulcerations present heal relatively quickly by means of simple outward applications, and mutilations, which in most cases result from neglect, are prevented.

As to the isolation of the lepers, it depends upon the social and political conditions of any given country as to whether it be made *obligatory* or *voluntary*. Isolation is urgently necessary in patients with nodular leprosy, particularly in the case of those afflicted with ulcerations. According to Sticker's investigations, also, the sufferers from the anæsthetic form are by no means so free from conveying danger as Impey asserts, and in their own interests as well as in the interests of the community, they should be sheltered in leper asylums.

In Norway, where such favourable results have been achieved, isolation has never been obligatory. A fairly sufficient segregation of the sufferers has been effected by the State bearing all expenses in connection therewith ; poor lepers are maintained at the cost of the State in State institutions, and are no longer permitted to be cared for on the farms as was done previously. The town councils also have power to enforce isolation to a certain degree in the case of lepers who wish to stay at home. It is necessary for such patients to have their own room, or at all events their own bed and bedding, which must not be used by anybody else. They are permitted to be in the same room, and to have their meals at the same table as the healthy inmates of the

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[1] The Matoonga Leper Asylum near Bombay is a pattern asylum on a large scale ; besides the sick wards, there are shops belonging to it, a hospital, a pharmacy, a school, a Hindoo temple, a Mohammedan mosque and a Roman Catholic church.

house, but have to possess their own utensils, crockery, &c. If these conditions are not complied with after repeated warnings, the patients are removed to a public leper asylum or hospital. At stated times the isolated patients are permitted to leave the leper asylum to make small purchases in the town. Marriages amongst lepers are also permitted.

The voluntary segregation of lepers according to the Norwegian pattern was recommended to all nations, with self-government and a sufficient number of doctors, at the Leprosy Conference in Berlin.

The non-isolated lepers as well as all suspicious persons—that is to say, all who have come into close contact with lepers or have lived with them a long time—must be subjected to continual sanitary police supervision, for which purpose it is, above all, necessary to *register lepers* and to *notify every case*.

A further requisition which should be carried out in the interest of the public is that leprous persons should be forbidden by law from begging in the streets, frequenting inns and places of public resort, using public wells, baths and privies, or tramping the country as beggars or pedlars ; moreover they should not be allowed to hire themselves as servants, and should be prevented from keeping shops, or carrying on the occupations of barber or laundry-man ; in fact they should be excluded from any calling relating to clothing and food, and also from prostitution.

The ulcers of the sufferers, from which quantities of bacilli are discharged, must be covered with *protective dressings*, and old dressings should be burned. Particular attention should be paid to the *nasal* and *pharyngeal secretions*, and also to the *expectoration*, which should be suitably disinfected.

The clothing, bed and bedding of lepers must be disinfected, and should in no case be used by other persons. Their *dwellings*, likewise, must be disinfected.

In non-leprous countries the sanitary police should keep under supervision *lepers who have arrived from abroad*, this at the present day being no rarity on account of the commercial intercourse, more especially in the principal commercial centres. Such persons should not be lost sight of, and should be prevented from mixing unnoticed amongst the population and kindling centres of infection. Soldiers, sailors and colonial officials coming from leprous countries should be subjected to examination.

Particular attention should be directed to the *wholesale emigration* from *leprous countries*, such as takes place from over-populated India and China to countries in which labour is required. Chinese coolies undoubtedly conduce enormously to the spread of leprosy, especially around the coasts and islands of the Pacific Ocean. Control should be exercised not only at embarkation, but, above all, over ports of disembarkation ; and the lepers should be examined by the Consular authorities of that country to which the emigrant is bound.

TREATMENT.

Up to the present time there is no known specific treatment for leprosy. The *serum therapy* with which Carrasquilla is supposed to have attained good results in Columbia has not stood the test. As the leprous bacillus cannot be artificially cultivated and no animals susceptible to leprosy are known, the first conditions for testing the efficacy of serum therapy are lacking. No object can be attained in making immune animals still more immune by the injection of leprous material.

Carrasquilla prepared his serum from the blood of horses into which the blood of lepers had been repeatedly injected. Herman and Abraham, and others, injected the tissue fluid of leprous persons into the animals, the blood of which was used for the preparation of the serum.

As is the case with all diseases which are difficult of treatment, the number of remedies for the cure of leprosy that have been tried and recommended and again cast aside are legion ; it is impossible in this work to mention all of them, so I must confine myself to the description of the principal remedies.

Iodide of potassium has usually a markedly toxic effect on lepers. During the administration of the drug there occurs a more or less serious eruption of nodules accompanied by fever, a symptom which is observed within a few days after doses of 0·1. Danielssen, therefore, used iodide of potassium as a means of testing supposed cures (Holst).

The recognition of the infectious nature of the disease suggests the use of *disinfectant remedies*. Labbé praises the efficacy of *carbolic acid* (used externally and internally). I tried this in the form of subcutaneous injections (in 1 or 2 per cent. solution, 4 to 8 daily), and although in one of my cases I continued this treatment for eighteen months, I was as far off getting good results as other persons. Westerland and Danielssen give a favourable report of *salicylate of soda*. Danielssen uses it in both forms of leprosy. He commences with 1·0 administered four times daily and gradually increases the dose, and in conjunction therewith adopted periodical blood-letting by means of cupping glasses (four to six every fortnight), and baths (vapour baths alternating with tub-baths and sea-baths), and he asserts that if the patients come under treatment early, a cure is effected in many cases. Weber, in one case of nodular leprosy, observed that improvement set in by means of Priessnitz's dressings with 10 per cent. salicylic acid in spirit, with baths of permanganate of potash ($\frac{1}{2}$ to 1 per cent.). I observed no results from the use of salicylic acid. Langerhans recommends *creosote* in pills ; Danielssen, however, found it had no effect. Doutrelepont applied 1 per cent. sublimate dressings, and inunction with 1 per cent. sublimate lanoline ointment, and under this treatment he observed that many nodules disappeared or suppurated and healed. Crocker, in two cases of the nodular form, saw improvement result after intra-muscular injections (buttocks) of hyd. perchlor. (0·18 : 15·0 ; one injection once or twice a week) in addition to the internal administration of chaulmoogra oil.

Gurjun oil or balsamum dipterocarpi, and *chaulmoogra oil* (from the seeds of gynocardia odorata, Lind. ; a tree growing in Assam and the Indian Archipelago) hail from the East Indies and are used internally and externally. Of gurjun oil 2·0 to 8·0 is given daily, pure or with lime-water (bals. gurjun 15·0, pulv. gu. arab. 7·5, aq. calcis ad 200·0, one tablespoonful three times daily). With chaulmoogra oil one starts with three minims three times a day, increasing the dose gradually till from 30 to 50 minims or more are taken three times daily (Bälz gave up to 15·0 per day), given in milk, or better still in gelatine capsules after meals. Externally both these remedies are used in the form of liniments, Gurjun oil with lime water (1 : 1·3) or lanoline (āā) ; chaulmoogra oil with oil (1 : 10-20) and both should be rubbed in twice daily, for fifteen to twenty minutes at a time. Tourtoulis also used chaulmoogra oil in the form of subcutaneous injections (5·0). Improvement but no permanent cures were accomplished with both these remedies, both of which were at first highly praised ; the effect of the rubbing itself plays an important part in all inunctions. I have used gurjun oil in many cases but without

attaining any permanent results. *Tai-fushi*, which is identical with chaulmoogra oil, is much esteemed by the Japanese.

A new remedy called *hoang-nan*, which is derived from strychnos gautheriana, growing in one of the mountain forests of Assam, hails from Tonquin. Brassac gave it a trial; he administered it in the form of pills of 0·1 mixed with realgar and alum, one to seven daily; the results he achieved, however, were not very encouraging.

Beauperthuy recommends cashew nut oil, from the pericarp of anacardium occidentale, Linn., a large tree which is very common in the West Indies; it is applied externally to the nodules, on which it is supposed to act as an irritant, causing them to become smaller or even to disappear entirely. Danielssen, after using this oil, not only saw no improvement, but in one case there was even an aggravation of the disease.

Kalindero found pure petroleum most useful (internally in capsules of 1·0-1·25, four to six daily; externally as a 10 per cent. to 20 per cent. ointment).

The efficacy of *reducing measures* is particularly claimed by Unna. This observer combined several remedies by having different parts of the body simultaneously rubbed with ointments of pyrogallol (5 to 10 per cent.), chrysarobin (10 per cent.), and ichthyol (10 to 50 per cent.), ichthyol being at the same time taken inwardly (1·0 per day). By means of this treatment Unna "cured" one case. The patient came to Germany from Brazil for treatment, but after returning to Brazil the disease reappeared, as was confirmed by Azevedo Lima and Havelburg, and the patient died of leprous-cachexia two years after her return. Dreckmann asserts that he also cured a case by means of Unna's treatment, 10 per cent. pyrogallol and chrysarobin ointment, salicylic-creosote-chrysarobin plaster externally, and ichthyol internally. Unna, found the treatment of separate nodules with salicylic-creosote-chrysarobin plastermulls very effective, and ichthyol useful in bringing the pigmented skin back to normal. Recently Unna has recommended oxydised pyrogallol (6·0 daily, 5 per cent. salve), which prevents the disagreeable accessory effects of ordinary pyrogallol. Danielssen, who has had great experience and during his practice of more than fifty years has methodically tried every new remedy for leprosy that sprung up, has certainly observed fluctuations in treatment by these methods, that with inconsiderate rapidity have been looked upon as cures; but as such apparent improvements set in after all methods of treatment, and even without any treatment at all, he found that no permanent usefulness resulted from any of them.

Europhen has recently been recommended by Goldschmidt. He uses it in the form of injections and inunctions of 5 per cent. solution of oil, and asserts that by these means he cured one case of the nodular form. Danielssen used europhen without result, as well as hydroxylamin, aristol, naphthol, salol and methylene blue, internally and subcutaneously.

Fornara recommends *airol* used externally as a powder or 10 per cent. ointment and subcutaneously in the form of a 10 per cent. emulsion of oil (1 drop to 1 syringe). Maitland, in two cases of nodular leprosy, saw some results from *thyroid gland* (using the raw thyroid of the sheep pounded with sugar and water); Manson found wonderful improvement was attained in a case of nerve leprosy by a three years' use of *thyroid extract*, but Brieger found it useless, as also was *thyro-iodine* or *iodo-thyrine*.

As the muscular substance is the only material of the human body immune to the bacillus lepræ, Voorthius, by Unna's advice, made a trial of intravenous injections of *Valentine's meat juice*. This experiment was carried out in Deli (Sumatra) on four Chinese. The meat juice was

diluted with equal parts of artificial serum (0·2-1·0 every two days) and caused an improvement in the general state of health, as also swelling and reddening of the nodules, which afterwards became softer and were absorbed, or were emptied by incision.

Dyer attained remarkable results with Calmette's *antivenene* (see poisoning through snake venom) in four cases out of five, after Carreau had observed that the nodules had disappeared from a leper after the bite of a rattlesnake.

Experience gathered from the use of different remedies have thus taught us that transient improvement (especially the disappearance of nodules) can be achieved with many remedies, but in spite of all a real cure is far distant.

The tuberculin "fashion" led to treatment of leprosy with *tuberculin.* It was proved that in lepers as in consumptives a general as well as a local reaction to it set in.   Under this treatment it was observed that there was improvement and even cure (Truhart), whilst other authorities (Danielssen) found that the treatment aggravated the disease.   It may be supposed that by now the preliminary enthusiasm has evaporated.

The observation made by several doctors that an improvement of symptoms occurred in lepers after having had a typical attack of erysipelas, led Havelburg to experiment with *inoculations of erysipelas* and with Emmerich's serum ; the result, however, was a complete failure.

Attempts have been made to effect improvement in leprosy by operative means, such as *excision of the nodules, nerve stretching, suture of nerves* (Bomford), *division* and *scraping out* of the diseased nerves (Cramer). The results, however, achieved by these operations were, as may be conceived, not considerable.   Operation wounds in lepers are known to heal remarkably well, which fact has probably some connection with the diminished sensibility (Bälz).   Forming eschars on the nodules with corrosives (Unna particularly recommends a paste composed of caustic potash and quicklime), the use of the thermo-cautery or the galvano-cautery, are some of the methods resorted to.

Disinfectant local treatment of the ulcers by antiseptic dressings is of importance in preventing pyæmic conditions from being set up.   This procedure also renders the infectious secretions of the patients harmless to persons around them.

According to A. v. Bergmann's experience ulcers heal quickly under treatment with Schede's sublimate powder.   Bälz' advice is to scrape out and then wash out bad-looking ulcerations and then to fill them with salicylic acid ; less severe ulcers should be powdered with salicylic acid with talc or starch (1-5 : 20).   Miller saw rapid results from chinosol in torpid ulcers.

In *perforating ulcerations of the soles of the feet* it is advisable to excise the disease tissue around the ulceration, or to completely remove it with the sharp spoon and to bandage it antiseptically.   Rake found the following proceeding successful.   The scalpel is passed through from the sole to the dorsum of the foot and all the tissue is divided to the edge of the interval between two toes.   If the ulceration is situated near the edge of the foot the scalpel is conducted laterally ; the wound is then packed with lint, when healing by granulation results.

V. Petersen recommends pure lactic acid for the *local treatment* of the *diseased mucous membranes.*

In order to prevent adhesions of the iris with the lens in leprous affections of the *eyes*, it is advisable to instil atropine; sometimes also iridectomy is indicated.   Moreover, when there are nodules on the cornea the

Showing results of Amputation for perforating ulcer of the foot in Lepers.　Photograph by EDWARD HORDER, F.R.C.S.Edin.

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clear parts anterior to the nodules should be incised (to check their growing inwards from the conjunctiva to the cornea) ; the excision of the nodules, or the application of the thermo- and galvano-cautery is also recommended. When the lower eyelid has dropped or become everted through paralysis, a plastic operation, which, according to Hansen and Looft, is to be performed at the outer and inner canthus, will be found of service. At the outer canthus the usual process is adopted, but at the inner canthus the margins of the eyelids internal to the puncta lachrymalia are laid bare by very superficial incisions and then the bared edges are united by two sutures. When the lid has only dropped a little the operation at the inner canthus alone suffices. Should the power of vision be lost and severe supra-orbital neuralgia still persist, the eyeball must be enucleated.

In disease of the *larynx*, tracheotomy may become necessary when attacks of suffocation set in and emetics are of no avail.

I successfully combated *pains in the diseased nerves*, which are occasionally excessively severe, by the application of the galvanic current, anode on the nerves, cathode on the sternum. It is also permissible in such cases to try the anti-neuralgic drugs, such as antipyrin, antifebrin, phenacetin, &c. Bälz effected the relief of neuralgia in one case by opening the nerve sheath and injecting 5 per cent. carbolic acid between it and the nerve substance.

In *attacks of fever* that did not yield to the usual remedies, Müller found chinosol (1·0 per diem in divided doses) very effective.

General treatment should not be undervalued. Nourishing food, suitable to the condition of the digestive organs of the patients, should be given ; as tonics—such as iron, quinine, arsenic, cod liver oil. Simple warm or hot baths (lepers feel a great want of warmth), and also salt water, alkaline, or sulphur baths decidedly exercise a favourable influence on the condition of the patients.

The Japanese watering place Kusatsu, which possesses very strong hydrochloric-acid-sulphur-alum-iron springs, is the only place where Bälz has seen actual cures of leprosy.[1] Leprosy in this place is treated with hot baths and simultaneously with moxa. Bälz gives an interesting description of this hydropathic treatment :—

"The patient begins with three of these baths daily, and then five, during an entire month or even longer. The average number of baths is 130. The duration of each bath is naturally short ; in the hottest spring (over 50°) the maximum time is three minutes. Even this short time is torture to the patients, and in the particularly hot spring mentioned, the proceeding is conducted with strict military precision. Five times a day the trumpet is sounded ; then the patients assemble from all the inns in the middle of the village. The bath itself is the size of a medium-sized room, and is divided into three basins containing water at temperatures of 49°, 52°, 53°, into which fresh mineral water is constantly flowing. Over every basin at intervals of two feet there are planks on which the patients closely crowded kneel or crouch. Each person carries a ladle of the capacity of ½ l., with which he first of all pours water 100 times over his head. This drenching of the head with hot water before the bath is a wise provision as it prevents subsequent cerebral anæmia and fainting. The local hot head-bath has the effect of relaxing and dilating the vessels of the head, and without it there would be a severe rush of blood to the skin and muscular system, and the cerebral vessels would contract. The bathing master then asks : " Are you ready ? " and when " yes " sounds from every side he commands : " Into the bath, one, two, three," and with palpable exertion of will-power all the patients step into the water, which during the latter half of the cure, when great expanses of the skin are raw, is very painful. During the time they are in the water the bath master speaks to them, exhorting them to be of good courage ; sometimes he addresses them humorously, and sometimes in a singing tone. Sometimes he encourages them by the information that the greater part of the time has elapsed, for instance : " More than half the time is

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[1] *Verh. de xii. Kongr. für innere Med.* Wiesbaden, 1893, p. 410.

passed," "only one minute more," "only a second more," "be brave, hold out." Then when he calls out "finished," the people come out of the water looking exactly like scarlet fever patients, and go home to rest and to gather strength for the next bath.

About a week after the beginning of the cure, or a little later, a peculiar exanthem breaks out. not measles-like or acne-like, as in other sulphur baths, but purulent, similar to the pustules or pocks caused by tartar emetic ointment. It appears first where the skin is most tender and most exposed to friction, in the groin, on the scrotum, in the anal furrow, in the arm-pit, the bend of the elbow, between the toes, and consists of closely crowded groups of pustules which burst in the next baths, leaving a raw, red, suppurating skin surface.

If the baths are then discontinued this exanthem proves exceedingly stubborn. If, however, the baths are continued, notwithstanding the pain, the exanthem certainly often becomes more extensive, but in the third, fourth, or fifth week it begins to dry up. Then only is the cure completed, but the skin is still very sore and tender and painful, and boils or abscesses often break out.

The patients then betake themselves to an alkaline bath in the vicinity, that has the property, according to universal report, of alleviating the pains very quickly. In this stage the patient's skin has a scaly appearance. After another month all symptoms disappear.

This description suffices to demonstrate how energetic and difficult this hydropathic cure is. Therefore it is remarkable that the general condition of patients is but little affected. They have excellent appetites, and would feel quite well were it not that the itching is so severe as often to deprive them of sleep.

According to a report of Mr. Moore, communicated by Lewin, leprosy is often cured on the Fiji Islands as follows : The patient is exposed for a long time to the smoke of the burnt wood of the poisonous sinu-tree (Excoecaria agallocha L., a euphorbia growing in India, the Malay Archipelago, New Guinea, and the Islands of the Pacific Ocean as far as the Friendly Islands), and the skin is subsequently deeply scarified.

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XI.

FRAMBŒSIA TROPICA—YAWS.

DEFINITION.

Frambœsia tropica occurs endemically in the tropics, and is a contagious, chronic, infectious disease characterised by the appearance of raspberry-like papules on the skin. It bears some resemblance to syphilis.

NAMES.

The disease is known by different names in the different countries in which it is endemic. It is called *Yaws* (*i.e.*, strawberry)[1] by the West African negroes ; *Pian* (likewise strawberry) by the natives of the Antilles, and *Bubas* by Spaniards. On the Antilles and in Brazil ; *Lupani* or *Tomo* on the Islands of Samoa ; *Tona* on the Tonga Islands ; *Coco* or *Dthoke* on the Fiji Islands ; *Tonga* in New Caledonia and on the Loyalty Islands ; *Rucks* on Jaluit ; *Patek* in various places of the Dutch Indies ; *Amboinian pocks* (*Bouton d' Amboine*) on the Moluccas ; *Bobento* on Ternate ; *Puru* in Borneo and on the Malay Peninsula ; *Parangi* in Ceylon ; *Kwe-na* in Upper Burmah ; *Yang mey tcheang* in China ; *Gattoo* in various places of the West Coast of Africa ; *Framosi* in Calabar ; *Aboukoué* in Gaboon ; *Tetia* on the Congo Coast ; *Momba* in Angola. On the Gold Coast the Fanti designation is *Dube* or *Dubea ;* the Accra name is *Ajortor ;* and the Haussa name *Tongara* (Prout).

The designation *Frambœsia* (from framboise, raspberry) was bestowed on the disease by Sauvages in 1759. Charlouis, on account of the many significations of the word frambœsia in medical terminology, has suggested the designation *Polypapilloma tropicum*.

HISTORY.

The first notification of the disease came to Europe at the commencement of the sixteenth century (1525), through Oviedo, who became acquainted with it in St. Domingo, and who referred to it under the Spanish name *Bubas*. Reports followed from Brazil by Piso (1648), from the Indian Archipelago by Bontius (1718), and from the West Indies by Pater Labat (1722). In recent years the geographical distribution and the pathology of the disease has become more generally known.

It is questionable if the disease described by the Arabian doctors Avicenna and Ali Abbas in the tenth century under the names *Safat* or *Sahafat* relates to frambœsia, as is asserted by some ; more probably the disease referred to was syphilis (Hirsch).

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[1] According to Nicholls the name *yaws* is derived from the Celtic word *ias*, which means to " well up."

YAWS.
Photographs by P. B. COUSLAND, M.B., Swatow, China.

GEOGRAPHICAL DISTRIBUTION.

Frambœsia only occurs in tropical countries.

The tropical regions of Africa form its principal seat, and it occurs on the West Coast from Senegambia to Angola (it was not observed in Cameroon by F. and A. Plehn), in the district of West Soudan (Timbuctoo, Bornu), Algiers, the bed of the Nile, Mozambique and the African Islands, the Comores, Madagascar and Mauritius, where, however, Prout found no typical cases of the disease, but only crab yaws (see below). Lately Griffiths has observed yaws in South Africa (Kimberley), Kaffirs being affected by it there.

In Asia, the following places belong to the geographical region of distribution of frambœsia: the Malabar Coast, the Coromandel Coast (Pondicherry), Assam, Ceylon, Upper Burmah, Siam (Rasch), the Malay Peninsula, the Indian Archipelago, the Moluccas and China.

Moreover the disease is endemic on a few groups of Pacific islands ; on the Salomon Islands, New Caledonia, the Islands of Fiji, Tonga, Samoa, and on Jaluit (Marshall Islands).

The islanders of Fiji have almost all yaws in their childhood. They have the belief that a child, in order to grow up healthy, must have this disease. They therefore inoculate those children with yaws that do not get it naturally.

In America, where it was probably carried by the negro slaves, yaws is known in the Antilles, and in Brazil, Venezuela, Guiana and Costa Rica.

ETIOLOGY.

Yaws is infectious, and the contagion is contained in the secretion and blood of the papules of the patients, as confirmed by inoculatory experiments on persons. Inoculation " takes " on healthy persons, and also on yaws patients, whose illness is not influenced thereby.

Micro-organisms have been found in yaws by many observers. The discoveries, however, do not coincide with each other. It is therefore doubtful if any of the microorganisms hitherto discovered are the ætiological factors in the disease.

Eijkmann found *short rods* in fresh papules of yaws; they were easily cultured on the usual nutritive medium and only liquefied gelatine slowly. Inoculatory experiments with them as well as with the diseased tissue itself were negative. Breda came across *bacilli* also in sections of tissue ; these were partly situated in blood vessels, but were never intra-cellular.

Pierez, on the contrary, discovered enormous numbers of *micrococci* in the papules as well as in the blood, and he succeeded in culturing them in beef tea and on nutritive gelatine which was superficially liquefied by them.

Nicholls, in conjunction with Watts, also found *micrococci* in the papules and their secretions, which he succeeded in culturing; he also found them in the lymphatic system and in various organs of a case that he examined *post-mortem*. The same microorganism was also confirmed in the dust on the floors of rooms in which yaws patients lived. Nevertheless experimental transmissions made on animals with pure cultures yielded negative results.

Hirsch also succeeded in five cases in culturing micrococci resembling those described by Pierez from the secretion of papules, and of four fowls inoculated with these cultures one developed typical yaws.

Natural transmission takes place by means of injuries of the epidermis, superficial wounds, ulcers on the legs and feet, chaps on the hands, the nipples of nursing mothers, or the angles of the mouths of children, scrofulous eczema, &c. ; each and all may form the point of entrance for the virus of disease. Transmission may be also effected by means of flies and other insects, and also through clothes, mats, and the soil and walls of dirty, infected huts, &c.

The degree of contagion of the disease does not seem to be the same in different countries. It is reported that it is so contagious on the Fiji Islands that Europeans acquire the disease by passing the night in the houses of natives (Skottowe).

The *period of incubation* is differently given by different authors; it appears, from the accounts furnished, to fluctuate between two weeks and two months. After inoculations the period of incubation is between twelve and twenty days, and is therefore shorter than when the disease is naturally acquired.

Once the disease has been got over, protection is afforded for a long period, or for ever.

There seems to be no heredity, and children are never born with the disease.

Hallen observed an infant with yaws twenty days after birth. He was born with an eruption resembling prickly heat on the fourth finger of the left hand and on the back, from which the papules developed. The mother suffered from yaws. Hallen is of opinion that the child was infected at the time of birth or subsequently.

No *age* is spared by the disease; the age of childhood is, however, principally affected. A few observers saw the disease in children exclusively.

Both *sexes* are affected without distinction.

Black and *coloured* persons are more frequently attacked than white persons and those of mixed races, a circumstance that is attributable to the fact that the whites bestow more care on their skins; and as they live under more favourable hygienic conditions the possibility of infection is less than is the case with the black and coloured races. Hirsch, however, does not consider this reason suffices for the explanation of the exemption of the white races, and he instances an observation of Ferrier, who knew several white persons who did not acquire the disease in spite of the intimate connection they had with sick negresses and mulatto women. This observation is in direct opposition to the fact respecting the Fiji Islands mentioned above.

The influence which, according to Keelan's observations, *vaccination* exercises on yaws is interesting. If vaccinated persons are taken ill with yaws the disease has a very mild course. Vaccinations made on persons suffering from yaws have no local results, but exercise a favourable influence on the course of the disease.

A form of yaws also occurs in *fowls*, in which Pierez discovered a micrococcus similar to that in human yaws. It is, however, questionable if the two complaints are identical. Hirsch states that he several times caused typical yaws in fowls by inoculating them with the secretion of yaws-papules.

SYMPTOMATOLOGY.

The disease usually sets in without prodromata; occasionally, however, the outbreak is preceded for a few days by *prodromal symptoms*, which consist in indefinable sensations such as are apt to usher in other infectious diseases; these are general languor, fever, headaches, uneasy sleep, delirium, pains in the limbs—particularly the joints—gastric disorders, constipation, giddiness, palpitation of the heart. In negroes the skin loses its usual gloss and becomes dull and sometimes scaly and lighter in colour.

YAWS.
Photograph of a Hindu suffering from Yaws, contracted in Fiji.
By H. N. JOYNT, M.A., M.D., Fiji.

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The actual illness, according to Rat, begins at the inoculated spot with the appearance of a *papule*, which after about a week begins to burn, and after another week is transformed into an ulcer which, heals, leaving an insignificant superficial cicatrix. This *primary affection*—which, according to Thorpe, is usually situated on the feet, legs, or perineal region—is frequently overlooked; it may, however, be lacking, as proved by Paulet's inoculation experiments, or it may resemble the efflorescences of the secondary eruption. The secondary eruption may immediately accompany the primary eruption, or may only set in when this has been present a long time, or when it has already healed up.

The *secondary eruption*, which is sometimes more widely, sometimes less widely, scattered over the body, consists of *papules* which, at first sight, are of the size of a pin's head, grow gradually, attain the size of a pea or small nut, and through confluence with neighbouring efflorescences may become as large, or larger, than an apple—so large in fact may they become that they sometimes cover the whole cheek, the knee, or the dorsum of the foot. The skin in the meantime becomes thinner and finally broken or shed, when a shiny red verrucous split surface is revealed (in much reduced patients this is dull white or dirty yellow) which in its appearance resembles a raspberry. It exudes a whitish-yellow, sero-purulent fluid which dries up into yellowish eschars, or if mixed with blood and dirt the scabs may be of a blackish colour. If these are removed new crusts form again and again; if left on they gradually assume a conical form resembling rupial scabs.

The papules are usually round or oval in form, and may become irregular in shape through confluence with neighbouring efflorescences. Where exposed to pressure, as on the thigh and in the armpits, they become flattened and remind one of syphilitic condylomata. Their consistency varies; they are sometimes hard, sometimes soft. They are generally not sensitive, except that they cause pain when situated on the soles of the feet or palms of the hands, where the eruptions cannot easily force their way through the thick epidermis, or when their seat is beneath the nails of the fingers and toes; as a rule, however, they cause a troublesome itching. It must be remarked, moreover, that the patients disseminate a peculiar rank, repugnant odour.

According to Milroy these papules are occasionally preceded by dryness of the skin and dark brown spots covered with fine white scales, which are mostly seen on the forehead, neck, chest, forearms and legs. They remain for a few days and disappear with the outbreak of the papules. They may be repeated before each relapse, and sometimes they remain during the whole period of illness.

The papules are by predilection situated on the face, on the mouth, nose and eyes, or on the neck, the limbs, the anus, and the sexual parts, while the trunk and the hairy part of the head are more rarely affected. At the edges of the nails of the fingers and toes the papules cause paronychiæ similar to those met with in syphilis.

The *mucous membranes* may also become the seat of papules; they are, however, principally observed on the orifices lined with mucous membrane, namely, the nose, the lips, or the vulva. One or two observers (Milroy, Breda) have also seen papules on the conjunctivæ, the gums, the tongue, in the pharynx, the larynx, and in the trachea.

The number of papules may vary considerably. Occasionally there are only isolated eruptions, which the English call "*mother-yaws*" and the French "*maman-pian*," the primary affection being by others com-prehended under this designation. Sometimes also large, persistent

papules are called *mother-yaws*, *grandmother-yaws*, and *maman-pian*, while smaller ones are called *daughter-yaws* and *granddaughter-yaws*.

The first eruption is frequently followed by one or several *relapses*, which are again preceded by fever and pains in the limbs. During the relapses, and in the intervals, inoculation of the disease still succeeds, whereas this is not the case when it is definitely extinguished (Gewand).

Various observers have mentioned the appearance of *swellings of lymphatic glands*, which may be painful to the lightest touch. Sometimes the centre of a gland suppurates, but the pus becomes re-absorbed ; in other cases they may break and discharge pus.

In the further course of the disease the papules gradually become pale and dry up, forming hard eschars which at last fall off leaving slightly thickened spots that may remain evident for years, and which in negroes are lighter than the surrounding skin, but in whites are mostly darker. Real cicatrices do not form when the healing takes place naturally. Recovery generally ensues with the disappearance of the eruption.

In some cases—particularly in patients who are afflicted with a constitutional disease such as scrofula, syphilis, scabies, &c., owing to which they are much enfeebled—the papules become enlarged and are transformed into large irregular ulcerations, which by predilection are situated on the limbs, and becoming deeper, lead to caries, gangrene, and the loss of toes. When healed they leave irregular radiated scars, which, when situated in the vicinity of joints, may cause contractions and ankyloses.

The following are symptoms which sometimes develop during cases of long duration : painful periostitis, caries of bone, fibrinous articular inflammations setting in with rheumatoid pains, which hinder the function of the limbs, and sero-fibrinous teno-synovitis. Such occurrences, however, are not symptoms appertaining to frambœsia, but are probably the manifestations of coincident ailments. Gewand states that the above symptoms have not come under observation of late years, that is, since iodide of potassium treatment has been generally adopted for yaws patients.

In most cases the general condition of the patient undergoes no essential disturbance except during the symptoms that precede the eruption, and for a short time afterwards. The complaint terminates in recovery. Little children may die of exhaustion if the fever at the commencement of the illness is high and the treatment unsuitable (Däubler). Death from exhaustion may also ensue in the case of patients in whom the development of ulcerations has taken place, but this is the consequence less of frambœsia than of some constitutional disease simultaneously present.

In rare cases the fatal termination is brought about by the appearance of pyæmia, septicæmia, or phagedæna.

According to Spire, yaws is the chief cause of *infant mortality* in the district of Uaddah (Upper Ubangi in French Congo).

Sometimes for a considerable time after all other symptoms have vanished, only one or two papules remain which are apt to be called *membra* yaws, "membra" being the negro abbreviation for remember.

The *duration* of the disease varies between a few weeks and several years. The treatment, food and hygienic conditions of the patients influence the time the disease lasts.

The following *varieties* of yaws differ from the normal type of eruptions :

(1) *Crab yaws* (*tubboes, tubba, crabs, crappox, crabes* in the West

YAWS.

Photograph of a Hindu woman, showing stains left by eruption when faded as well as some active granulomata, contracted in Fiji.   By Dr. H. N. JOYNT, Fiji.

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Indies, *boeboel* in the Dutch Indies). This form occurs on the soles of the feet and the palms of the hands, and in consequence of the thickness and hardness of the epidermis at these places having an obstructive effect on the development of the papules, severe local inflammation is set up. Crab yaws is characterised by ulcerative fissures of the skin, out of which the characteristic proliferations rise. When the epidermis is not completely broken through, but only sieve-like openings or fissures are found through which a copious exudation runs, it is called *running crab yaws*.

(2) *Ringworm yaws*.—This designation is used when the papules are arranged circularly and are confluent, so that a ring, reminiscent of herpes tonsurans, is formed. The same appearance is present when large papules have healed up in the centre.

(3) *Pian dartre* (in a few West India Islands) or *yaws cacca* (in Jamaica) is the name given to the illness when, instead of papules, yellowish spots appear which exhibit small punctiform protuberances covered with minute dirty-white scales.

(4) *Pian gratelle*.—In this variety, which sometimes follows an ordinary eruption, there are small, slightly raised blisters in lieu of the papules.

PATHOLOGICAL ANATOMY.

Anatomical examination of the diseased tissue reveals the fact that frambœsia is a chronic dermatitis, that takes its point of departure from the papillary layer of the skin, and leads to the formation of excrescences.

According to Unna, the epidermis is found to be much thickened, and in a few places migratory cells and fibrinous coagulations are lodged. The papillæ are elongated to ten or twenty times their usual length, and the blood vessels in them are dilated, as they are also in the thickened cutis. The cutis and papillary bodies contain a solid cellular infiltration, which principally consists of fine large plasma cells. This cellular infiltration is mostly situated round the dilated veins, but shows no relation to the hair follicles and sweat glands. The hair follicles and the hair itself is normal, but the sweat glands are dilated and their epithelium somewhat enlarged. The musculi erectores pilorum were found by Charlouis to be very hypertrophic. The raspberry shape of the papules is owing to the circumstance that after the removal of the superficial cutaneous coverings the enlarged papillæ of the dermis are revealed. The papules of yaws in their formation closely resemble syphilides, particularly the condylomata.

As to the condition of the *internal organs* in yaws, hitherto there has been but little information ascertainable. Van Leent found the lymphatic glands enlarged and partly caseous, and besides, there were caseated tubercles in the liver, spleen, kidneys and lungs. Rake in three cases demonstrated simultaneous tuberculosis of various organs, but in a fourth case all the viscera were normal. Tuberculosis has nothing to do with yaws ; it appears as a complication only.

DIAGNOSIS.

The diagnosis of yaws is not attended by much difficulty. Confusion with other diseases, amongst them syphilis, is hardly possible. Formerly yaws was taken for a form of syphilis (Alibert). This opinion, however

—apart from all other considerations—is contradicted by the fact that the two diseases may simultaneously affect one person; clinical observation and inoculation experiments have demonstrated this : syphilitic persons in all stages of their disease can be infected with frambœsia and *vice versâ.*

Hutchinson considers yaws to be the original disease from which the European syphilis has been evolved ; according to his opinion the two diseases have become modified by having been propagated by different races.

PROGNOSIS.

Yaws is for the most part a slight ailment followed by spontaneous cure. It has only an unfavourable termination in the case of little children and patients who are simultaneously suffering from some severe constitutional disorder.

PROPHYLAXIS.

Protection is most effectually secured from the disease by personal cleanliness and care to avoid injury to the epidermal covering. Yaws patients should be isolated and their dwellings, as also their clothes and other property, should be disinfected.

In Ceylon, according to Wright, a sort of *inoculation* takes place, rice being given to children off the same plate or leaf from which a sufferer from yaws has eaten. The children subsequently develop yaws severely, and are cured from it in about a week by treatment with small doses of mercury. This is supposed to diminish the severity of subsequent attacks.

TREATMENT.

Cleanliness is the principal requisite of treatment, and is best carried out by daily warm baths and washing with soap. Warm clothing, avoidance of chills, warm drinks are indicated, and easily digestible and nourishing foods.

Of all drugs iodide of potassium is most highly recommended, whereas mercurial preparations are not borne so well. The use of arsenic and of iron and quinine is advisable for weak and anæmic patients, and persons with badly-developed and pallid eruptions.

Locally the papules should be cleansed with solutions of sublimate or carbolic acid, dabbed with liquid carbolic acid, or with sulphate of copper, the application of tincture of iodine, and if the excrescences are of long standing they should be scraped out with the sharp spoon. Mense found the local application of a thick paste composed of moistened subnitrate of bismuth most efficacious. Hirsch recommends 1 part lactic acid to 8 parts of ungt. hydrargyri nit. Hæmorrhages should be treated with styptics or compression.

In *crab-yaws* the thickened hard epidermis should first be softened in warm water, or by means of poultices, and after cutting away the softened skin the sulphate of copper pencil should be applied.

Ulcers should be dressed antiseptically.

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XII.

VERRUGA PERUVIANA.

DEFINITION.

By the term Verruga Peruviana is understood a general chronic infectious disease characterised by persistent fever leading to anæmia, and followed sooner or later by the appearance of peculiar wart-like protuberances on the skin and in the organs. This disease mostly occurs in certain high valleys on the western declivities of the Peruvian Andes.

HISTORY.

The history of verruga peruviana extends back to the sixteenth century. Zarate of Lima made mention of this disease in his History of the Conquest of Peru published in 1543.

GEOGRAPHICAL DISTRIBUTION.

Verruga was formerly distributed in Peru over a wider area than at the present day. At the present time its occurrence is confined to a few valleys in the Departments of Ancachs and Lima, situated between 8° and 13° south latitude on the western declivities of the Andes.

The infected districts are narrow valleys shut in between mountains, and watered by small streams which overflow at certain seasons. The valleys, especially when they run parallel with the coast, are not reached by the winds from the sea nor from the mountains, and their climate is therefore characterised by great warmth. Owing to this circumstance, along with the fact that they are abundantly supplied with water, they rejoice in an exuberant and really tropical vegetation. The valley of the Rimac through which the railway from Lima to Oroya runs is the principal centre of verruga.

The disease is not equally distributed in the valleys, verruga-affected villages in them alternating with verruga-free villages.

Probably the disease is not confined to Peru. Some time ago De Havilland Hall[1] published a short note on "a peculiar disease" which occurs in Zaruma, in Ecuador, and is seemingly identical with verruga. Firth is of opinion that it is also endemic in Bolivia and the northern part of Chile.

[1] *Lancet*, November 10, 1883.

ETIOLOGY.

Verruga peruviana is *not* considered contagious by the native doctors. The *transmissibility* of the disease was proved by the unfortunate experiment of a young Peruvian doctor in Lima, Daniel Carrion. In 1885 Carrion inoculated himself in both arms with the blood from a verruga excrescence ; after a period of incubation of twenty-three days he developed the disease, and he succumbed to it fifteen days later. The disease is therefore also called *Carrion's disease* in his honour.

In Peru it is universally believed that the disease is originated by drinking the *water of the verruga-affected districts,* or by bathing in it. The waters that flow through the valleys in question are therefore called " aguas de verrugas."

It is probable that, as in yaws, injuries of the epidermal covering form the channel by which the virus of the disease gains entrance. Chastang mentions that recently many observers consider the thorns of the cactus opuntia to be the cause of the disease, because the pricks from this plant cause corneous warts. According to Chastang's opinion, parasites clinging to the thorns may probably affect the question.

The nature of the *virus of disease* is still unknown. It is true that various observers have discovered *micro-organisms* in the excrescences, and in the blood and organs of verruga patients, but it is doubtful if these are really the cause of the disease.

Izquierdo found *bacilli* between the cells and fibres of verruga nodules ; the vessels of the diseased parts of the skin were crammed full of them, and the vessels of the healthy skin and subcutaneous cellular tissue also contained them. Besides the bacilli *cocci* were found.

Florez, from the blood of a verruga patient, cultured cocci which were mostly united in chains.

Odriozola discovered *bacilli* of various sizes and granulated appearance in the blood of feverish (not in afebrile) patients ; he succeeded in culturing them in bouillon, but two inoculatory experiments on dogs with cultures turned out negative.

Finally Nicolle and Letulle, working independently of each other, found bacilli lying separately which morphologically resembled tubercle bacilli ; Nicolle found them in miliary nodules in the lung, liver, spleen and lymphatic glands, Letulle in epidermal nodes, particularly in the subcutaneous cellular tissue (the preparations had been sent to him from Peru). The bacilli were mostly free between the cells, but were also found isolated in mononuclear phagocytes (Nicolle) and in capillaries (Letulle).

Moisture and *warmth* seem to play an important part in originating the disease, as may be gathered from the description of the condition of verruga-affected areas. *Malaria* is an almost inseparable concomitant of verruga, and bears a certain relation to this disease. In April, when the rivers that have overflowed their banks begin to retreat, the cases of disease from malaria as well as from verruga increase. The turning of the soil, incident to the construction of the railway from Lima to Oroya, was followed by a severe epidemic of verruga. Frequently the two diseases were complicated, and malaria doubtless plays no insignificant part in the invasion fever, more especially the so-called Oroya fever (see below).

In order to decide the question as to what degree malaria participates in the genesis of the invasion-fever, it would be advisable to make experiments on animals (conducted in malaria-free places) which, as verruga is considered to be transferable and also to occur amongst animals (see below), promises conclusive results. Blood-examinations should also be undertaken, although Odriozola in thirty cases of verruga fever found no malaria parasites.

Altitude seems to be of less consequence to the occurrence of the disease than to its course. The verruga areas are situated at altitudes of from 400 to 3,000 m. Along the littoral the cases that occur have all been imported.

Incubation, according to Odriozola, averages from fifteen to forty days. Other observers state that it may drag on for months or even a year.

Recovery from the disease mostly confers immunity. Relapses seldom occur, accessions of the illness during the course of the disease must not be regarded as relapses.

No *sex, age* or *race* can claim immunity from verruga. Newly-born infants may even be severely attacked; sometimes infants are born with the disease upon them.

Acclimatisation plays an important *rôle*. The natives of the valleys, where verruga is endemic, or persons who have lived there a long time, are seldom attacked, but natives of other districts and foreigners are attacked frequently and severely. Odriozola does not believe that the negroes are immune; they very seldom venture into verruga districts.

Persons occupied in *earth-works* are particularly liable to attack. While the railway was being constructed, all the engineers and labourers occupied on the Oroya line were struck down by Oroya fever, and 50 per cent. of the engineers and 75 per cent of the European labourers succumbed to the disease.

Verruga is observed in various *animals*, especially horses, mules, asses, dogs and fowls. In horses, mules and asses in particular, tumours of a considerable size sometimes appear, this being the reason why large excrescences are designated *verrugas mulaires*. It has also been stated that animals suffer from Oroya fever.

SYMPTOMATOLOGY.

The picture of disease presented by Peruvian verruga passes through certain well marked stages. Three stages are distinguished: (1) the stage of invasion; (2) the stage of eruption; and (3) the stage of recovery.

The *stage of invasion* is introduced by uncertain symptoms, such as weariness of the limbs and indisposition. After these symptoms have been present a few days, slight rigors followed by fever set in during the afternoons or evenings. Soon the rigors become more severe and the fever increases. The fever is very irregular, being mostly remittent, seldom intermittent. When of an intermittent type, the attacks of fever are quotidian, more rarely tertian or irregular. Usually the intermittent fever later on becomes remittent. The temperature fluctuates between 38° and 38·5°, it seldom rises above 40°. Antúnez, however, mentions a case in which, during six days, the temperature was 42°.

The pulse is frequent, small and soft, sometimes dicrotic. The fever is accompanied by severe headaches, sleeplessness, pains in the back and limbs of varying severity, profuse night-sweats and sometimes also hæmorrhages, most frequently bleeding of the nose, more rarely petechial. The pains in the limbs are especially localised in the joints, and exhibit a great tendency to change their locality, and the pains become aggravated at night. The parts most apt to be attacked are the knee and ankle joints, and the small joints of the hands and feet. Painful contractions of certain muscles, particularly those of the calves of the legs, and often also of the sterno-cleido-mastoids, are observed; these spasms mostly appear at night. Occasionally the articular pains and muscular contractions are so prominent that the illness is mistaken for rheumatism. **The**

following further symptoms may set in : nausea and vomiting, giddiness, tinnitus aurium, flickering of objects before the eyes, photophobia, transient amblyopia, sensitiveness to sound, palpitation of the heart and carotids, dyspnœa and also slight bronchitis. In addition there is loss of appetite and great thirst. The tongue is coated, the bowels constipated at the commencement of the illness, but later on in the disease diarrhœa sets in, at first of a fæcal character, but later the evacuations are serous, and sometimes sero-sanguineous. The epigastrium and hypochondria are sensitive to pressure, the liver, spleen and lymphatic glands are mostly enlarged. The liver may be very considerably enlarged, but increase in size of the spleen is a less constant symptom. The urine is dark and scanty, depositing a sediment ; albumen is occasionally present.

One of the characteristics of verruga is that it induces marked auæmia. The higher the fever the more pronounced is the anæmia. The number of red corpuscles may be diminished to one and a half millions in the cb. mm., or less ; the skin becomes livid and sub-icteric ; the mucous membranes assume a waxy appearance. Anæmic sounds can be heard over the heart and cervical vessels ; there is frequently œdema, especially over the joints.

The prostration of the patients increases under the aggravation of the symptoms, and restlessness and slight delirium may set in. After this condition has persisted for some time—on an average from twenty-five to thirty days (Odriozola)—a gradual improvement of all symptoms takes place. The temperature becomes normal, or only slight irregular evening fever persists. This can go on for a month or longer, till the eruption appears and the disease enters its *second stage*. Sometimes it happens that the eruption immediately follows the invasion, with an improvement in the general condition of the patients ; or it may be that before the outbreak of the exanthem all the symptoms become still more pronounced, and only after the eruption has broken out does any improvement take place.

In yet another group of cases no eruption at all sets in, and after a general change for the worse death results, accompanied either by high fever, or the temperature sinks to normal or subnormal ; the latter are the more serious cases, and the fatal termination occurs from excessive exhaustion. Sometimes the fatal termination is attributable to complications affecting the lungs (pneumonia) or intestines (enteritis).

The form of fever in which the eruption stage is never attained, and in which death sometimes ensues after a few days, is generally known as *Oroya fever* on account of its having come under observation amongst the labourers and engineers engaged in the construction of the Oroya line. Odriozola gives it the name of *Fièvre grave de Carrion*.

The symptoms of the stage of invasion are not in all cases so pronounced as have been described above. It is not uncommon for the only symptoms to be general languor and weakness, indisposition, great apathy, slight headache and low fever.

Odriozola states that the average duration of the first stage of the disease is between three and four months.

The *second stage* starts with the outbreak of the *exanthem*, the pathognomonic symptom of the illness. As already mentioned, death often occurs prior to the appearance of the eruption ; on the other hand it seldom happens that the disease runs its course without an eruption. The eruption commences with small slightly raised pinkish-red spots, which are soon transformed into dark red, or dusky bluish papules, which in their turn become wart-like excrescences. Sometimes small shiny

blebs, similar to sudamina, in other cases larger blisters and pustules, or even petechiæ, form the point of departure of the exanthem.

The eruption may, however, extend over the entire surface of the body, but it is the face, neck, and limbs that are especially attacked. The parts of the face chosen by predilection are the forehead, the superciliary arch, the eyelids, cheeks, nose, chin, and ears : on the limbs the extensor surfaces and the vicinity of the joints are affected to the greatest extent. The palms of the hands, the soles of the feet and the hairy part of the head may become the seat of the eruption, while the trunk is hardly ever attacked. Often the growths appear symmetrically, and sometimes injuries favour their outbreak on those parts of the body thus affected.

The *number* of excrescences differs considerably ; sometimes there are only a few of larger or smaller dimensions, sometimes a large number, and they may become confluent to such an extent that almost the entire · skin is covered.

Their size is quite as variable ; at times they are so small that they might be mistaken for sudamina, in other cases they may attain the size of a small apple. The small excrescences are situated in the superficial layers of the skin, the larger ones in the deep layers and in the sub-cutaneous cellular tissues ; the latter are therefore at first only perceptible to the touch, and the skin over them is unchanged.

Odriozola distinguished two forms according to the size of the excrescences, the *forme miliaire* (from the size of a pin-head to a pea) and the *forme mulaire* (larger) ; nevertheless these forms are not specifically different from each other.

As to their *form*, they may be cylindrical, conical, globular, semi-globular, fungiform, or of irregular shape ; when several excrescences are confluent they are generally of an irregular form. Moreover they may either have a broad base or be pedunculated.

Sometimes the places on which the eruption breaks out are œdematous, and this is especially the case when the eruption is severe ; this is most frequently observed on the legs.

When the verrugas have attained a certain size their surface appears smooth and glossy. Their consistence varies, being hard, soft, or fluc-tuating. As they are rich in blood vessels they easily bleed. They then become pale and exhibit reddish or blackish dots or eschars on their apices. These hæmorrhages, which, if considerable, still further conduce to make the anæmic patients still more bloodless, occur more frequently at high altitudes in consequence of the rarefication of the atmosphere, than in the more low-lying places; the course of the disease on the whole is more rapid in high than in lower altitudes.

Not only is the skin the seat of these new growths, but the eruptions extend to the mucous membranes and internal organs. There exists no mucous membrane or organ in which they may not appear, and the symptoms they can originate are remarkably manifold. Thus excrescences in the nose may cause epistaxis ; in the throat and œsophagus, dys-phagia ; if situated in the larynx, cough, hoarseness, hæmoptysis, and even suffocation may result ; if they have their seat in the lungs hæmop-tysis and infiltration may set in, which may be mistaken for tuberculosis; when situated in the stomach they cause hæmatemesis ; in the intestine, diarrhœa and intestinal hæmorrhage ; in the kidneys or bladder, hæma-turia ; and in the uterus, metrorrhagia. In rare cases the brain and spinal column participate in the disease, inducing epileptiform convulsions and symptoms of meningitis. The diagnosis of " inward " verruga, when the eruption is not simultaneously present on the skin, is sometimes extraordinarily difficult.

The eruption seldom develops all at once, but generally in *successive crops*, each of which is preceded by a rise of temperature.

Sometimes the eruption is *abortive* and consists of slight elevations of a pale-red or light-grey colour, which become dry and horny reminding one of real warts. These soon disappear and are apt to be followed by a slight bran-like desquamation.

The general symptoms which may have improved prior to, or after, the outbreak of the eruption again become worse, and not infrequently attain an intensity equal to that observed during the first stage. They may even become so severe that death ensues. Profuse sweats are an important symptom exhibited by patients during the entire course of the disease, and they do not cease even when there is no fever, appearing especially at night and increasing when new growths appear.

The duration of the stage of eruption is long and tedious. In consequence of renewed outbreaks, it may drag on for over two years. On an average, however, according to Odriozola, it lasts four to six months.

In the *third stage, the stage of cure*, the eruptions disappear, the general symptoms improve and convalescence sets in.

The eruptions disappear in various ways: by (1) *simple involution*, (2) *ulceration*, and (3) *suppuration*.

In the first case the excrescences become smaller, turn pale, and are covered by scales, which are cast off, leaving a brown spot for some time, but no scar. This process is sometimes accompanied by violent itching.

Ulceration occurs particularly in large excrescences. These become soft and disintegrate, causing occasionally abundant hæmorrhages; they then present the appearance of spongy protuberances that bleed easily, and exude a sanguineous, purulent, fœtid fluid; they are of a red, grey, or blackish colour, resembling ichorous, malignant masses. If the secretion dries up they become covered with brownish scabs, and finally they heal by cicatrisation.

Suppuration of the excrescences is seldom observed.

The duration of *verruga peruviana* varies considerably. Carrion died on the sixteenth day of disease. Generally, however, the disease extends over months or years.

The *termination* of the disease is frequently unfavourable. In natives the mortality averages about 10 per cent. It is higher in whites and may increase to 40 per cent., or even to 85 or 90 per cent. in Oroya fever. Death may be caused by the severity of the infection, exhaustion, or septicæmia.

PATHOLOGICAL ANATOMY.

The bodies of persons who have died of verruga peruviana exhibit *great pallor* of all the tissues and organs.

Hyperæmic or inflammatory centres are frequently found in the *lungs*, particularly at their bases.

The *heart* is pale, flabby and shows fatty degeneration.

The *liver* is enlarged, more or less brittle, slate-coloured.

The *spleen* is soft, mostly enlarged, but sometimes shrunken.

The mucous membrane of the *intestine* is occasionally hyperæmic. The solitary follicles and Peyer's patches are generally enlarged. Sometimes ulcerations are discovered in the intestine, as well as in the stomach (ulcerated verrugas).

All the *lymphatic glands* appear swollen, the mesenteric glands more especially so.

The *bone marrow* is hyperæmic and of a spongy consistence.

Verruga excrescences are naturally the most important condition, and these are met with not only *on the skin*, but are largely distributed in the *interior of the* body. According to Odriozola, they have been found on the mucous membranes of the eyes, nose, mouth, throat, œsophagus, stomach, intestine, larynx, trachea and bladder; on the serous membranes, the endocardium, in the cerebral and spinal meninges, and the choroid plexuses; in the lungs, liver, spleen, pancreas, kidneys, testicles, muscles, periosteum and probably in the bone marrow. The following organs and tissues also become affected: the lymphatic glands, the thyroid gland, the cellular tissue behind the eyeball, the cellular tissue of the vertebral canal, the adventitia of the blood-vessels, the articular and peri-articular cartilages. The internal growths, however, never attain the size of the external; according to Odriozola, they always belong to the miliary form and are situated in the interstitial connective tissue.

As to the *microscopic* appearances of the *excrescences of the skin*, they mostly consist of cells of various kinds: mono- and poly-nuclear leucocytes and swollen connective tissue-cells which are kept together by an exceedingly delicate fibrous stroma. They contain numerous vessels the walls of which are infiltrated with leucocytes, and in larger growths the centre is cavernous. Probably the rarification of the atmosphere in high altitudes exercises some influence on the existence of this cavernous tissue. The fat-cells of the subcutaneous cellular tissue, as well as the sebaceous glands, hair follicles and sweat glands, are completely included in the infiltration. In non-ulcerated growths Letulle found the skin attenuated and infiltrated with leucocytes and the papillæ obliterated; in ulcerated growths, on the other hand, the skin, where it was still extant, was hypertrophic and the papillæ elongated, the cells of the malpighian layer were proliferated and leucocytes appeared between them. In the neighbourhood of the ulcers the papillæ had disappeared, and here and there, in the vicinity of the ulcerative surface, there were agglomerations of pus.

The miliary papules of the *internal* organs examined by Nicolle consisted of epitheloid cells surrounded by embryonal cells, and in some parts exhibited caseation and giant cells. Letulle, on the other hand, found neither caseous areas nor giant cells in the papules of the skin. It is therefore by no means beyond the bounds of possibility that—taken in conjunction with the presence of bacilli mentioned above—the case from which the preparations examined by Nicolle originated was not a case of verruga, but of tuberculosis.

DIAGNOSIS.

In the stage of invasion the diagnosis of the verruga disease is often very difficult. Confusion is possible with malaria, acute hepatitis, pyæmia, acute miliary tuberculosis and acute articular and muscular rheumatism.

A previous stay in a verruga infected district is of great importance in the history of disease. The enlargement of lymphatic glands, which is apt to subside after the eruption breaks out, is of great diagnostic value.

Once the eruption has appeared the diagnosis presents few difficulties.

For only one disease, *yaws*, may *verruga* be mistaken, when the diagnosis is not aided by the place of observation; the appearance and distribution of the exanthem exhibits great similarity in the two diseases.

To a superficial observer it might appear that the two diseases are very different, but on more minutely considering the subject it will be found that the differences are only a question of degree, with the exception that hitherto no internal manifestations have been observed in yaws, and that verruga may be present at birth. I am therefore inclined to the opinion that the two diseases are nearly related, verruga being nothing more than *a severe form of frambœsia or yaws, modified partly by the high altitude of the regions where it occurs and partly by being complicated with malaria.*

PROGNOSIS.

The prognosis of verruga, particularly as regards whites, is always serious. The following symptoms, according to Odriozola, may be regarded as *favourable :* The general appearance of the eruption, immediately after the usual symptoms of invasion ; also when the excrescences develop to a certain degree and then slowly subside, while the general improvement takes place quickly. The prognosis, on the other hand, is *unfavourable* when the eruption, be it partial or general, pales quickly and disappears without the general condition improving.

TREATMENT.

The first line of treatment is to *remove the patients from the verruga infected district* and, when possible, to bring them to the coast. In other respects the treatment is *symptomatic*, and is principally directed to the fever, pains and anæmia. On account of frequent complication with malaria, Odriozola recommends that quinine be tried in every case.

The *local* treatment is the same as in yaws. Odriozola advises that all ulcerated protuberances should be extirpated or removed by ligature.

The natives attribute a specific effect to a decoction of *maize* and a decoction of *Buttneria cordata*, both of which possess diaphoretic qualities.

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XIII.

THE PONOS OF SPETZA AND HYDRA.

DEFINITION.

Under this title Karamitsas and Stephanos have described a disease occurring on two islands, Spetza and Hydra, that are situated near the coast of Argolis. It is an endemic chronic disease commencing with fever and considerable enlargement of the spleen. It only occurs in children, and has usually a fatal termination. At present its occurrence on the above-mentioned islands is comparatively rare ; formerly the disease was of much greater frequency.

SYMPTOMATOLOGY.

The disease begins acutely with fever, which is also maintained during the course of the disease. The children become languid, sad and disinclined to play, and their complexion assumes a pale, yellowish colour. The appetite is not lost, and is even sometimes increased to morbid hunger, highly seasoned foods and spirits being particularly craved for. The digestion, however, is always disordered ; at first there is usually constipation, and sometimes vomiting is observed. The spleen becomes enlarged and frequently attains an enormous size, so that it may reach to the median line of the abdomen. It is frequently painful, either idiopathically or upon pressure ; it is seldom quite painless. For this reason the disease is called *Ponos* (pain). The liver is only exceptionally slightly enlarged The abdomen is distended with wind. The urine from the commencement of the disease has a decided odour, and the same persists during the course of the ailment. Albuminuria very seldom occurs. In rare instances enlargement of the cervical glands has been observed. The fever exhibits an intermittent or irregular type. The condition rapidly becomes worse, the children become more and more emaciated and bronchitis frequently sets in. Broncho-pneumonia, peritonitis and meningitis are rarer complications. In place of the costiveness at the commencement of the disease, profuse diarrhœa may set in later on, or the stools may assume a dysenteric character. After a longer or shorter period dropsy supervenes, with œdema of the face and limbs, and later ascites occurs. Moreover, hæmorrhages in the skin, from the nose, the intestine, and above all from the gums (which have a scorbutic appearance) are of frequent occurrence. Hectic fever and profuse perspirations are further concomitants, and the children at last succumb owing to exhaustion.

Recovery is but seldom observed. The duration of the disease generally averages one to two years; sometimes, however, it does not exceed two or three months.

PATHOLOGICAL ANATOMY.

Hitherto we know but very little of the pathological anatomy of the disease, as we have only the report of one *post-mortem* examination made by Stephanos.

In this case the spleen was enlarged, but not much pigmented, the trabeculæ and stroma were considerably thickened, and the capsule very firm. In the right lung an abscess was found reaching to the pleura. The liver exhibited initial cirrhosis (alcoholic drinks had been given to the child in the course of the disease). The kidneys were hyperæmic; and isolated bronchial and mesenteric glands were swollen.

ETIOLOGY.

The etiology of ponos is quite obscure. Climate, season, or condition of the soil are supposed to exercise no influence in the genesis of the disease. Food and social condition play no part in its origin. Rich and poor are equally attacked. It occurs in healthy houses as well as in the hovels of the poor. Only *children of the tenderest* age are attacked by the disease, which mostly develops whilst the first incisors are being cut. Children of 4 years of age or older are very seldom attacked. The male *sex* is attacked somewhat more frequently than the female.

The disease is mostly confined to families with a tubercular history, and in these it is not rare for several children to be seized.

Further researches are urgently required, and should be directed to find out if malaria parasites are present, and to confirm whether ponos is a specific infectious disease or only a *phase* of *malaria*, which, as is well known, has a predilection to attack very young children.

TREATMENT.

Treatment consists in giving the sufferers *suitable* food (in the case of sucklings a good wet nurse should be obtained), and tonics (quinine, iron, iodide of iron) should be administered. One cannot, however, build great hopes on the results of these measures.

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II.—DISEASES CAUSED BY INTOXICATION.

I.

PELLAGRA.

DEFINITION.

Pellagra (from pelle agra, *i.e.*, rough skin) is an exceedingly chronic disease, attributed to eating spoiled maize, and of the nature of an intoxi· cation. It runs its course in attacks which are manifested by gastric and intestinal phenomena, nervous and psychical disturbances, and by the appearance of an erythematous exanthem. In its further course this disease mostly leads to general cachexia and to a fatal termination.

SYNONYMS.

Malattia della miseria, Mal del sole, Malattia dell' insolato di prima-vera, Risipola lombarda; Mal de la rosa, Mal roxo, Mal de Asturias (Spain); Maïdismus, Psychoneurosis maïdica, Raphania maïsitica, Lepra italica, Scorbutus alpinus.

HISTORY.

The history of pellagra cannot be traced back further than to the first half of the eighteenth century. The first news of the disease came from Spain, where, according to the report of Casal in 1735, it appeared endemically in a district of the province of Asturia, and thence spread over the northern provinces of Spain. Soon after the disease appeared in Italy. Even previously to 1750 it was first observed in the neigh-bourhood of Sesto Calende by the Lago Maggiore, and during the next few years it spread over Lombardy, Venice, Emilia, Piedmont and Liguria, and later on also ap-peared in Central Italy. In about 1820 it appeared in the south-west of France, and in the forties in Roumania and in Corfu. Recently, endemic centres of pellagra have also been discovered in Austria, Russia and Portugal, and reports have also been pub-lished of the endemic occurrence of this disease in other countries besides those of Europe.

GEOGRAPHICAL DISTRIBUTION.

Pellagra prevails endemically in Europe, Africa and America.

In Europe its geographical region of distribution extends over North Spain, North Portugal, the South-west of France, North and Central Italy, South Tyrol, the district of Goerz-Gradiska, Bosnia, Hungary, the Transylvanian districts, the Bukowina, Roumania, Moldavia, those parts of Russia bordering on Roumania, especially Bessarabia and Corfu.

In Spain the provinces of Asturia and lower Arragon, Burgos and Guadalajara are the principal seats of the disease.

In France it prevails principally in the Departments Gironde and Landes; smaller centres are found in the Hautes et Basses Pyrénées, Haute Garonne and Aude.

In Italy, Lombardy, Venice and Emilia are the principal centres. The provinces of Brescia, Padua, Ferrara and Piacenza are most severely affected, over 5 per cent. of the rural population suffering from pellagra.

According to the official statistics published by the Minister of Agriculture, the number of persons suffering from pellagra in Italy in 1881 was 104,607 = 0·36 per cent. of the total population; of these 55,881 = 2 per cent. of the total population belonged to Venice, and 36,630 = 1 per cent. of the total population to Lombardy. About 10 per cent. of the persons afflicted with pellagra are mentally disordered. In the Italian lunatic asylums there is an average of 10 sufferers from pellagra to every 100 patients, in Venice 35, and in Lombardy 15. Between 3,000 and 4,000 persons yearly die from pellagra (Sormanni).

In Africa, Egypt, more especially lower Egypt (Sandwith) and Algiers, belong to the region of distribution of pellagra. In America, Mexico is its chief site, yet here in the native land of maize the disease is relatively rarely observed, and is principally confined to the southern provinces, Yucatan and Campeche (Vales).

ETIOLOGY.

Pellagra is a *disease of intoxication*, attributable to the continued eating for a considerable period of damaged maize (mais guaste). In those countries in which pellagra is endemic, maize forms the staple article of diet of the rural population, who are almost exclusively attacked by the disease. Maize for consumption is prepared in the form of pap made from maize-meal, the polenta of the Italians, the cruchade of the French, the mamaliga of the Roumanians, or in the form of bread. The maize used is often not quite ripe, is harvested and stored when damp, and thus easily becomes spoilt. It is this low class maize which the small agriculturists keep for their own use, while they sell the good maize. It is particularly in years in which there have been bad harvests and famine that this has been done, and for this reason the disease is particularly frequent in such years. In the warmer countries where maize is cultivated, such as in Mexico, Western Asia and India, the grain ripens and dries more easily in consequence of the more tropical climate, and therefore pellagra is either comparatively rare or does not occur at all.

The spirit (*brandy*) prepared from the unsound maize also appears to be capable of causing pellagra.

Opinions do not coincide as to whether the virus of disease is already contained in the unsound maize, or only develops in the body after the grain has been eaten. According to Lombroso, whose opinion is that it is contained ready in the maize before being eaten, and who has rendered great service through his investigations on pellagra, the intoxication is caused by the product of a chemical metamorphosis of the maize due to a micro-organism which *per se* is harmless. Lombroso succeeded in preparing a watery extract, an alcoholic extract, and a red oil by means of which pellagra-like symptoms could be originated in animals as well as in human beings. He conjectures that two toxins are contained in unsound maize, one an alkaloid resembling strychnine which is contained in the alcoholic extract and in the oil, and a narcotic substance resembling hemlock contained in the watery extract. Lombroso's investigations

have been confirmed in the works of Husemann and Cortes. Pellizzi and Tirelli, who lately were enabled to cause pellagra-like symptoms in dogs and rabbits through inoculating cultures of micro-organisms cultivated from unsound maize, ascribe great importance to the toxic effect of the products of metabolism of the micro-organisms themselves, which were very similar to the bacteria of decomposition. This conclusion was come to on the ground of their experiments. Neusser is of opinion that the toxin does not exist pre-formed in the maize, but only develops in the intestines, when the digestion is disordered, from a non-toxic substance which is digested and excreted when the digestive organs are healthy. Belmondo is likewise of opinion that the toxin is only originated in the body through the agency of micro-organisms which have been introduced into the system with the spoiled maize.

Various *fungi* found on maize to which some observers were inclined to attribute an etiological signification have proved to be harmless, at least in regard to pellagra. Balardini discovered a greenish fungus on mouldy maize which he believes to be capable of causing pellagra. It is called *verderamé* by this investigator, and *sporisorium maïdis* by Cesati. Lombroso, however, points out that this fungus is very rare ; in a journey through the whole of Lombardy he only once came across it. According to Lombroso this fungus is harmless and identical with penïcillium glaucum. The bacillus maïdis, which has often been found by Cuboni on unsound maize, and also in the fæces of persons with pellagra, is likewise harmless and, according to the investigations of Paltauf and Heider, belongs to the common potato bacilli. Two other fungi found on maize are the *maize-blight* (ustilago or cœoma maïdis) and the sclerotium maïdis. The former certainly has toxic qualities, originating a series of digestive and other symptoms, which, however, are quite different from those of pellagra. It is, moreover, only found in the western hemisphere (in Bolivia, Columbia), and therefore can have no etiological connection with pellagra. Carraroli in recent times found a bacillus in maize-meal which—or the product of decomposition of which—he considers responsible for pellagra, as, by means of subcutaneous injections of the toxic products, he succeeded in originating symptoms similar to pellagra in animals.

The *sporadic cases of pellagra or pseudo-pellagra* which have been principally observed in France, and which have no connection with bad food, have nothing to do with pellagra, it being in these merely a question of complex symptoms similar to pellagra, but of undoubtedly different origin (partly the result of chronic alcoholism). Husemann points out that possibly other substances, the constituents of which are similar to those of maize, may originate toxins with analogous effects under the influence of spontaneous decomposition. Examples of such are familiar in the case of salted and smoked fish, in which is developed a toxin analogous to sausage poison, or which in other cases are capable of originating choleraic symptoms due to a toxin analogous to a cheese poison, and yet in other cases cause urticaria and diverse skin eruptions.

Pons Sanz's report of the endemic occurrence of pellagra in the province of Badajoz (Spain), the inhabitants of which eat *no maize*, requires explanation.

The male and female *sexes* are almost equally attacked by the disease. During pregnancy and after parturition pellagra may develop.

No *age* is spared, but sucklings are exceedingly rarely seized. Persons aged between 40 and 60 years are most frequently attacked.

The *individual predisposition* is different. Although an entire family lives in the same manner only isolated members are attacked by pellagra.

Unfavourable hygienic conditions, bad food, alcoholism, enfeeblement through previous illnesses, are all *predisposing causes*. Pellagra has with justice been called a malady of the poor.

Winternitz goes so far as to deny the existence of pellagra as a specific disease peculiar to a limited area. What is described as pellagra is in his judgment only the conditions of disease induced by want and misery.

Heredity also plays a part in the etiology of the disease, as the acquired predisposition of the nervous system to contract pellagra can be transmitted to posterity. Lombroso is even of opinion that the disease itself is hereditary, especially from the grandparents.

SYMPTOMATOLOGY.

The symptoms of pellagra are so extraordinarily manifold that, as Lombroso expresses himself, " in no pathological condition can one say with more justice than in this that there are no diseases but only patients." There are even differences in the symptoms in different regions, some phenomena which predominate in certain localities being absent in others. This phenomenon may be possibly due to the different condition of the maize or the diet, or to climatic or racial factors.

Pellagra has a course distinguished by pronounced *attacks* alternating with periodical ameliorations and exacerbations. The exacerbations occur regularly in the *spring*. During the first attack stomachic and intestinal symptoms with nervous disorders set in, accompanied mostly by an exanthem. In the following attacks the disorders of the nervous system become more predominant and may cause a plurality of symptoms attended by a development of general cachexia. Tuczek, whom I principally follow in the following description, thinks it is convenient, like the first describer of this disease (Frapolli, 1771), to divide it into *three stages*, in spite of such division being somewhat artificial.

The *first stage* is apt to be preceded by prodromal symptoms for a longer or shorter period. According to Geber the patients for several previous winters feel languid without cause, they have no inclination for bodily or mental work and often complain of flying pains in the head, spine, or other parts of the body. With the advance of the spring these disorders diminish to again increase in the following winter. Thus it may go on for several years until, after a particularly severe winter, the distinctly pronounced symptoms of pellagra appear about April or May.

First of all *gastro-intestinal* disorders are set up : loss of appetite, disgust for food, particularly of maize gruel, more rarely bulimia ; moreover there is unquenchable thirst or an antipathy to drink, heartburn, eructation, abdominal pains. The tongue is coated, but during the further course of the disease its epithelium, partly or entirely, is shed. The region of the stomach becomes distended and painful. Diarrhœa is mostly present, and sometimes bloody stools are observed (v. Rosen) ; more rarely there is constipation. In a few cases Sandwith observed enlargement of both parotids without attendant pain.

These digestive disturbances are accompanied by *nervous disorders :* headaches, generally located in the occiput, giddiness and pressure in the head, vertigo, singing in the ears, sleepiness or sleeplessness, pains in the neck and back, a sensation of constriction, feebleness and uncertainty of movements, particularly of the legs. At the height of the attack the tendon reflexes are considerably increased. Moreover, there is usually sexual hypererethism, heightened psychical excitability, low spiritedness, weak memory, a difficulty in thinking, disinclination and disability for bodily and mental exertion, and not rarely a certain degree of mental obtuseness.

Simultaneously with these symptoms, though not constantly, an erythema appears. It particularly affects the backs of the hands, the lower third of the forearms, occasionally also the dorsum of the feet ; it also appears on the face, neck, and upper part of the chest—in fact on those places that are uncovered and exposed to sunlight. In the case of persons who, whilst labouring, go almost naked, such as the fellahs in Egypt, the greater part of the body is affected. The skin becomes red and swollen, causing the patient to experience a sensation of tension,
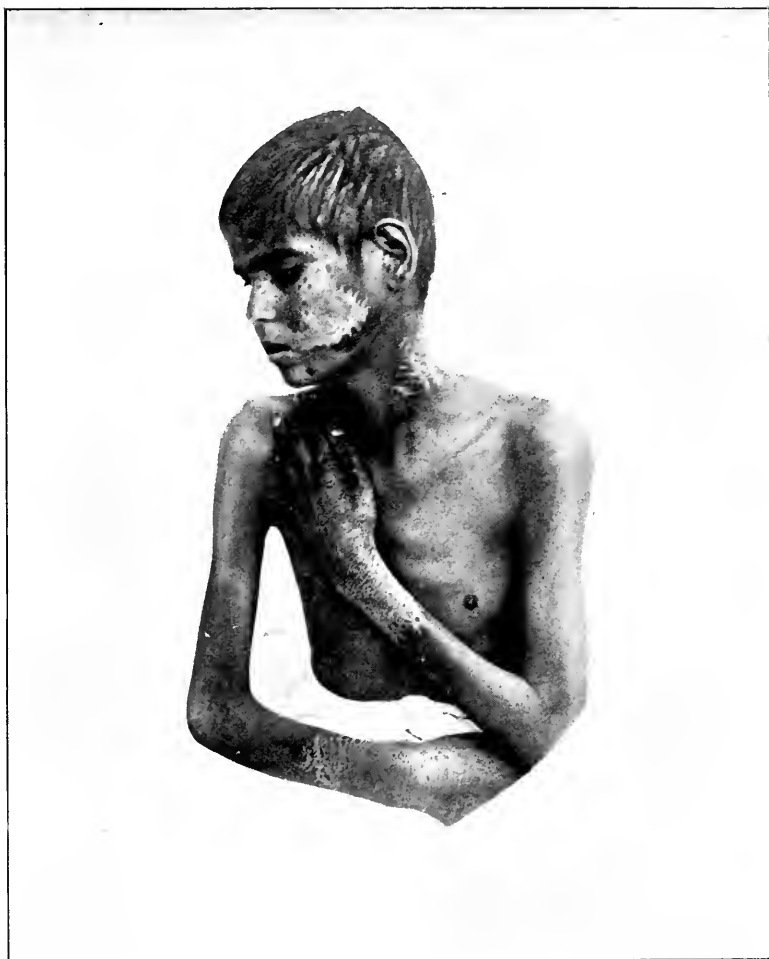
PELLAGRA IN EGYPT.
Photograph by F. M. SANDWITH, M.D., M.R.C.P.

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itching, or burning. Sometimes little blebs and pustules that dry up to scabs, or ezcema develops. After the erythema has subsisted for a few weeks a desquamation of the epidermis in large patches takes place.

After three or four months, therefore in July or August, the condition of the patients gradually becomes ameliorated; the skin, however, for a long time remains darkened, rough, and dry. In the next spring a fresh attack supervenes, and is generally more severe than during the previous year. The process is repeated in the following year, and the sequelæ left by the attacks become more and more considerable. The illness thus gradually passes into the *second stage*, which is characterised by the *serious cerebro-spinal symptoms* here enumerated :

1. *Motor Disturbances.*—There is usually a more or less considerable *muscular weakness*, particularly in the lower extremities. Occasionally there are partial *paralyses*, and in severe cases one-sided ptosis of the upper eyelid is observed ; on the other hand, according to Tuczek, ataxia does not occur.

The following motor *symptoms of irritation* are observed : muscular tension and tonic contractions of the upper and lower extremities, which may increase to tetanic rigidity ; sometimes also there is tremor of the arms, the head, and the tongue, likewise cramps, convulsive jerks, and uncontrollable movements of single limbs ; exceptionally, also, there are pronounced epileptiform fits with loss of consciousness.

The gait is either simply paralytic or paralytic-spastic. When, as happens in some cases, partial muscular atrophy sets in, the aspect of the disease is that of myatrophic lateral sclerosis, paralysis, contraction and atrophy of certain groups of muscles.

The *electrical excitability* of the muscles does not in every case exhibit changes. Lombroso often found that the flexors of the forearms were excited more easily than the extensors.

The mechanical excitability of the muscles is frequently increased, and idio-muscular contractions and fibrillary muscular twitchings also occur on mechanical stimulation.

(2) *Disturbances of Sensibility.*—The sensibility of the skin is unequal. The sense of touch remains intact, and also the sense of temperature, whilst much more frequently the sense of pain, particularly in respect to the legs, is diminished. The *muscular sense* is normal.

Parœsthesia is seen very frequently and in great diversity. The sensation of itching and burning on the trunk and extremities is the most frequent, and becomes so intolerable that it drives some patients to commit suicide. There is, moreover, the sensation of formication, subjective sensations of temperature (a feeling of flying heat, cold, or numbness), burning of the eyes, dragging in the neck, sensation of suffocation, a feeling of constriction about the chest, a feeling as of a band round the body, a sensation of weight in the region of the groins and uterus and of falling of the womb, a sensation of cold or of irritation or contraction of the penis and of heaviness in the testicles.

Besides the above-mentioned there may be experienced pains in the head, neck and back, and neuralgia, especially intercostal. Sandwith found sensitiveness to lateral pressure in the dorsal and lumbar vertebræ to exist to diverse extent, more particularly in the median dorsal region.

In regard to the *reflex* activity of pellagra patients, the skin reflexes are usually normal. The tendon reflexes are mostly increased, frequently to a considerable extent, particularly the knee-jerk ; very rarely, however, the patellar tendon reflexes are either weakened or quite absent.

(3) *Disorders of the Organs of Sense.*—Occasionally *weakness of vision, hemeralopia, diplopia, muscæ volitantes* and *photophobia*, are observed. The pupils, as a rule, react somewhat indolently. There is frequently dilatation, more rarely contraction of one or both pupils. *Ophthalmoscopically*, according to Lombroso, the conditions most frequently found are opacity of the retina and atrophy of the arterial vessels of the retina, more rarely atrophy of the optic nerve with or without retino-choroiditis, is found. Sometimes premature opacity of the lens sets in. Lombroso also observed blepharitis and pterygium.

The sense of taste is in some cases perverted: everything tasting "salty" to the patient. This is occasionally so predominant a symptom that the disease is named after it. Thus, the people of Lombardy designate the disease *salso*, while in Spain it is known as *flema salada*.

(4) *Vasomotor and Trophic Disorders.*—A general *state of contraction of the cutaneous vessels* has to be primarily mentioned, pallor of the skin, subjective and objective sensation of cold, and occasionally also goose-skin. During the later stages of the disease *neuroparalytic* dilatation of the capillaries and veins sets in, and also œdema. The face, more particularly the nose of the patient, is sometimes reddened, resembling the aspect of an alcoholic; indeed, complication with alcoholism is no great rarity.

The *skin eruptions* mentioned above must here be considered. Though doubtless the rays of the sun influence the eruption (on those parts of the fingers on which rings are worn the skin remains intact) [Scheiber], yet the solar influence only cannot be made answerable for it.

According to Bouchard the epidermis in pellagra has lost its fluorescence. In consequence the skin is deprived of protection from the chemical sun-rays, which —particularly the violet ones—tend to develop the eruption.

After repeated attacks the skin becomes of a brown hue and appears smooth, dry and thin; it also loses its elasticity, so that it may be lifted up in folds, which remain in position. White streaks resembling pregnancy lines may be present in the skin, whilst in other cases the skin appears to be infiltrated, fissured, and of a livid colour.

There are frequently disorders of nutrition of the *nails*. The nails are very rarely found normal in pellagra patients, being mostly clubbed, ridged, grooved, split, very thin, necrotic, or overgrown with skin.

The *tongue* frequently exhibits deep indentations and is deprived of its epithelium.

(5) *Psychical Disorders.*—There are, as a rule, some mental disorders in advanced cases of pellagra, principally of the nature of *melancholia*, with terror, delusions of guilt and persecution, which frequently, according to the religious standpoint of the population, take the form of monomania. The manifold paræsthesias from which the patients suffer sometimes cause hypochondriacal illusions. The perpetual presence of anguish and alarm often induces the sufferers to refuse food and seek self-destruction by drowning (hydromania). Actual, or sometimes seeming, *stupor* is a frequent peculiarity of pellagrous mental affection, and this is accompanied by obstinate dumbness. The sensation of illness is generally very pronounced in the sufferers, in some of whom consciousness is disturbed, sometimes to such an extent as to evoke delirium of a melancholic type. The melancholia, at first, is apt to appear *periodically*, and it is often only after the patients have had a yearly recurrence of the kind for a long period that insanity becomes *permanent*.

The mental disorder of the patients sometimes assumes the character

of *mania*, but this is less seldom the case than is the melancholic type. In some cases also mania and melancholia alternate with each other.

Uncontrollable ideas ("I am drawn into the water") occur in pellagrous patients—forced movements, forced positions, cataleptic symptoms and hallucinations, which may become manifest by delirium. According to Tuczek, however, pronounced paranoia does not appear.

If during the later stages of the disease the patients become imbecile, they remind one of sufferers from dementia paralytica, only the peculiar disturbances of speech and paralyses of the cerebral nerves are lacking, though veritable dementia paralytica also may occur in pellagra.

As to the remaining symptoms presented by the patients, the following are to be mentioned :

Increase of temperature may occur at the beginning, or at some period in the course of the disease ; the fever is, however, usually slight and very transient (Alpago-Novello).

The *pulse* is frequently accelerated, or it may be retarded.

The *gums* often exhibit a scorbutic diathesis.

The *gastric juice*, according to the investigations of Agostini, contains little or no free hydrochloric acid.

The quantity of *urine* is diminished, its specific gravity mostly decreased, its reaction often alkaline. Lombroso and Roncoroni found the excretion of urea, chlorides, and particularly of phosphoric acid, diminished. Albuminuria is seldom observed in Italy, whereas Dalla Rosa observed it in nearly half his cases in South Tyrol.

Brugnola states that he found *tyrosin* crystals in the urine.

Pellagra patients, moreover, markedly exhibit the signs of premature senility, such as premature greyness of the hair, baldness, wrinkles and lines on the face, loss of teeth, arcus senilis, atheroma, &c. (Alpago-Novello).

Should the disease break out in early childhood, there is *retardation* of *development* of the entire body, more particularly of the genitals.

In consequence of the disorders of digestion, the nourishment of the patient suffers in a high degree. Anæmia and emaciation become more and more marked, and the *third stage of disease*—the cachectic stage—is attained.

The marasmus persists and increases. The patients become permanently bedridden, bed-sores, paralysis of the bladder, uncontrollable diarrhœa, profuse mal-odorous sweats, weakness of the heart and dropsy set in, and the patients finally die of general exhaustion, or are carried off by intercurrent diseases, of which pulmonary phthisis or hypostatic congestion are the most frequent.

A peculiar typhoid condition, sometimes named *typhus pellagrosus*, occasionally closes the sad scene.

In the typhoid state there is an acute aggravation of all the symptoms, more especially the mental ; the consciousness becomes disturbed ; restlessness, delirium, and fever set in. The whole muscular system is in a condition either of rigidity or intense tonic contraction. The head is buried in the pillows, and at times convulsively moved. On spontaneous movement of the limbs a perceptible trembling and indications of inco-ordination are made manifest, and tremors and fibrillar contractions are seen in the face from time to time. The speech is drawling, tremulous and often exhibits a nasal twang. Frequently there is hyperæsthesia and increased reflex excitability, the tendon reflexes in particular are always increased.

The fever, which as a rule accompanies the typhoid condition, is very variable. The temperature, according to Belmondo, mostly fluctuates between 38·5° and 40·0°, and during the last days of life may rise still higher or, on the contrary, may sink far below normal.

Finally, fæces and urine are evacuated involuntarily; the tongue becomes dry and fissured, and sordes form on the teeth. The typhoid state may last a week or two, when death not infrequently results from lobular pneumonia.

Besides the fully developed forms of pellagra, *abortive* cases occur. Thus Scheiber observed cases in which the pellagrous eruption was the sole symptom; the eruption may disappear, or it may persist during the whole life without the disease ever assuming a dyscrasic nature.

The *duration* of pellagra is unusually variable. The disease may drag on for ten or fifteen years or more without even in this long period attaining its highest degree of development. But cases are also observed that are distinguished by a rapid course which may end fatally in three or four years, or even less. Recovery can only be hoped for in the first stage of the disease, when the patient has only had one or a few attacks, and is then permanently removed from exposure to the determining cause of the disease.

Sometimes pellagra exists in *conjunction with other* diseases, such as syphilis, scrofula and scurvy, the latter complication being called *scorbutus alpinus* in Italy. It may also be complicated with leprosy, this being frequently observed to be the case in the Spanish provinces of Asturia and Galicia.

PATHOLOGICAL ANATOMY.

The anatomical changes found in pellagra cadavers are manifold. These, however, are not wholly due to the disease itself, but to the general cachexia and the senile decay which it induces.

The cadavers, as a rule, are exceedingly emaciated, the panniculus adiposus and muscles wasted. Lombroso also sometimes observed brittleness of the ribs, though the condition of all other flat and long bones was normal.

The *heart* frequently exhibits brown atrophy, and more rarely fatty degeneration of the muscular fibres. On the whole, *abnormal agglomeration of* pigment—which otherwise is only peculiar to senile decay—is one of the most constant of the conditions found in pellagra; and pigmentation is present, not only in the myocardium, but also in the hepatic cells, the spleen, and the ganglion cells of the sympathetic, and in those of the anterior and posterior cornu of the spinal cord. The aorta is occasionally found to be atheromatous, and endocarditis is also sometimes met with.

The *liver* is frequently enlarged and undergoing fatty degeneration; sometimes brown atrophy is found.

The *spleen*, as a rule, is small and atrophic.

The *kidneys* frequently exhibit cirrhotic atrophy or fatty degeneration.

The wall of the *intestine* is thin in consequence of muscular atrophy, the mucous membranes of the rectum and colon hyperæmic and covered with ulcers.

The changes in the *nervous system* are the most important.

Hyperæmia, anæmia, and œdema are the conditions most frequently met with in the *brain* and *spinal column* and their *meninges;* chronic

inflammation of the meninges and sub-arachnoid hæmorrhages, changes which likewise occur in other chronic affections of the central nervous system, are met with. Sometimes, also, atrophy of the cerebrum, and especially of its cortical substance, is observed.

In regard to the *spinal cord* itself, Tuczek always found it diseased (in eight carefully examined cases). In all cases the *posterior columns* were the seat of symmetrical sclerosis, which extended more or less over the spinal cord, and especially involved Goll's columns. Besides these changes, in six cases there was symmetrical disease of a like nature in the *postero-lateral columns* corresponding with the track of the lateral pyramidal fasciculus. The changes, as a rule, were the most pronounced in the thoracic portion of the spinal cord, but the affection of the posterior columns mostly predominated over that of the postero-lateral columns. The posterior roots were intact. In one case Tuczek observed besides a degeneration of the anterior cornu in the lower portion of the cervical enlargement, and in a less degree also in Clarke's columns. The central channel in all cases was obliterated in its entire course.

The validity of Tuczek's examinations were confirmed by Belmondo, who also found disease in the pyramidal tracts and, more rarely, in the posterior columns likewise. Even before Tuczek's investigations were made Tonnini found degeneration in the spinal cord, especially in the lateral columns.

Vassale, by means of a particular method of staining, proved that the primary degeneration of the nerve fibres is not of a morphological but of a histo-chemical nature, the diseased fibres assuming a different stain to the healthy parts at a time that they still possessed their normal size and form.

According to these observations we have in pellagra to deal with a widespread disease of the spinal cord caused by intoxication, analogous with the affection of the posterior columns in ergotism and the lateral sclerosis in lathyrism (Tuczek).

P. Marie is of opinion that primarily there is disease of the cells of the lateral and posterior columns situated in the grey substance.

In the typhoid stage of pellagra Belmondo found acute myelitis accompanied by hyperæmia and infiltration of the spinal meninges. The changes peculiar to typhoid fever, such as swelling of the solitary follicles, Peyer's patches and enlargement of the spleen, are lacking.

The typhoid state in pellagra, according to Belmondo, is attributable to the blood being suddenly overloaded with a toxic substance which is either formed at one time in large quantities, or the excretion of which is prevented by the kidneys.

Marchi (according to Tuczek) in two cases of typhus pellagrosus found *micrococci* in the blood of the living as well as in the different organs after death ; Marchi, however, was unable to obtain cultures of these micrococci.

In regard to the *peripheral nerves,* Dejerine found the cutaneous nerves of the back of the hand degenerated. Raymond could not confirm this observation, and Tuczek, likewise, found the peripheral nerves normal. He even found no changes in the spinal and sympathetic ganglia with the exception of the above-mentioned agglomeration of pigment.

DIAGNOSIS.

The diagnosis of pellagra presents no difficulty in pronounced cases. Nevertheless the features of the disease are sometimes not so well marked but that the correctness of the diagnosis may be doubted. The statements

of the patients must be taken into account as to the course of the disease
and the periodicity of the symptoms.

The exanthem is moreover of great diagnostic value, but as we have
seen, this symptom is not always present.

Typhus pellagrosus may give rise to confusion with acute infectious
diseases, uræmia, and diabetic coma.   The differential diagnosis consists
particularly in the non-typical course of fever, the negative condition of
the organs and urine, and the absence of an acute eruption.

PROGNOSIS.

The prognosis of pellagra is generally unfavourable.   More minute
information, however, is given in the symptomatology.

PROPHYLAXIS.

In order to prevent the disease, care should be taken that *unsound
maize is used neither as an article of food nor in the preparation of brandy*.
Importing, selling, or making flour of unsound maize should be prohibited ;
provision should be made for the supervision of spirit distilleries in which
maize is used, and for the supervision of the importation of brandy from
pellagra districts.

Care must moreover be taken that maize is only planted in those
districts in which the grain can become quite mature.

Maize which has been harvested damp is to be well dried before being
stacked, and for this purpose the erection of suitable *kilns and well-
ventilated granaries* is advisable.   In the south of France this proceeding,
according to Gubler, has had the best effect, pellagra having quite
disappeared after the introduction of ovens for drying the grain.

Improvement of *hygienic and social conditions*, which, as we have seen,
play an important part in the etiology of the disease, is another prophy-
lactic requisite.

TREATMENT.

The patients, above all, must be deprived of the cause of their disease,
and in the place of unsound maize a *generous and nourishing diet*, con-
sisting chiefly of meat and milk, must be substituted ; there is no objection
also to sound maize.

As to *drugs*, Lombroso recommends the administration of *arsenic*, with
which good results have been obtained.   It is given in the form of Fowler's
solution, 5 drops daily, increased gradually to 30 drops.

Lombroso warmly recommends that young patients should be rubbed
with salt water.   Mineral waters containing sulphur are recommended for
baths and internal administration.   Agostini advises that the stomach be
washed out with salt water, and that hydrochloric acid be given after meals.

In other particulars the treatment is symptomatic.   For combating the
giddiness Lombroso recommends tincture of cocculus (5 to 10 drops
daily).   As a specific for the diarrhœa Cerato advises airol (0·03-0·04 to be
taken three or four times daily for a week or two).   The spinal symptoms
are treated with salt water baths, massage, and electricity.

The *diseased parts of the skin* are anointed with carbolic, boric, or zinc ointment. The torturing itching and burning are relieved by cool baths and spongings; friction with carbolic acid water (2 per cent.), inunctions with carbolic ointment (4 per cent.), cocaine ointment (1·3 per cent.), menthol liniment (2·5 : ol. oliv., lanolini āā 25·0), or painting with equal parts of hydrate of chloral and camphor, have all something to recommend them in the treatment of pellagra.

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II.

LATHYRISM.

Lathyrism (Lathyrisme médullaire spasmodique), so called on the suggestion of Cantani, is a disease with a spastic spinal paralytic course, and which is attributable to poisoning with various kinds of the family of the Papilionaceæ lathyrus (chick pea or common pulse).

HISTORY.

The disease was probably known to the ancients—at least it may be inferred from the fact that, according to Huber, in the Hippocratic writings on epidemics this disease is referred to as follows : '' At Ainos those men and women who continually fed on pulse were attacked by a weakness in the legs which remained permanent ; but even those that lived on peas (ὄροβος) suffered from pains in the knees.''

Lathyrism, there is not a doubt, was observed in Italy (Modena and Tuscany) and France (Moempelgard) during the seventeenth and eighteenth centuries. During the nineteenth century, also, the fact that lathyrism attacked a large number of persons in France, in British India and in Algiers, caused attention to be directed to the study of the disease. Amongst other places in India, the disease appeared in Pergenna-Barra in 1857, when 2,028 persons—more than 3 per cent. of the population—were attacked by it (Irving).

In India the lathyrus is called *kesari* or *teori*, in Algiers *djilben*, and lathyrism *meurd-djilben*, *i.e.*, the chick-pea disease.

GEOGRAPHICAL DISTRIBUTION.

The disease hitherto has been observed in several departments of *central* and *south France*, in *Italy, Algiers* and *British India*.

ETIOLOGY.

Lathyrism is a *disease of the nature of an intoxication*, which may be originated by eating *various kinds of lathyrus*. Of these the *lathyrus sativus* L., *lathyrus cicera* L., and *lathyrus clymenum* L., come principally under consideration. The herb lathyrus belongs to the order of leguminosæ ; it is cultivated in various countries, and is principally used as food for cattle. Under certain circumstances, especially when the harvest is bad and famine exists, lathyrus is used as an article of diet by human beings, a flour made from the grain being mixed with corn meal, and bread prepared therefrom.
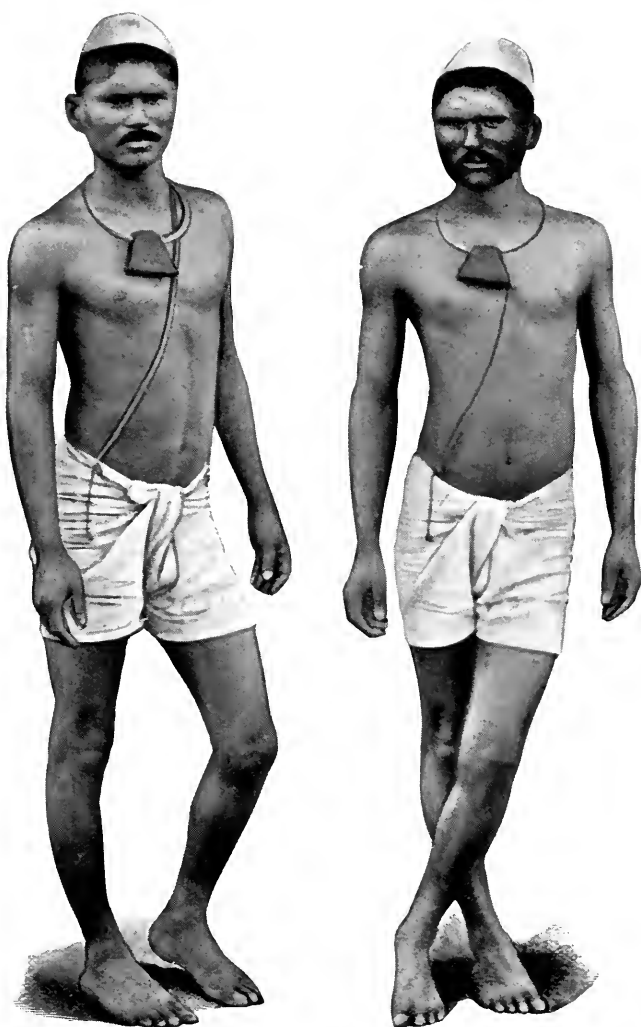
LATHYRISM.

Photographs illustrating the paralysis resulting from the prolonged use of Lathyrus Sativus as a food in India.   By Captain W. J. BUCHANAN, I.M.S.

By kind permission of the Proprietors of " The Journal of Tropical Medicine."

The poison is actually contained in the healthy grain, so there is no question of the grain being diseased or rotten. The lathyrus is a herb that is principally grown on swamp soil and only developes in certain years. Its chemical composition is hitherto unknown. It is true that several poisonous alkaloids have been extracted from its grains, but further investigation is required. By the administration of preparations made from the grains, a disease giving rise to symptoms similar to lathyrism has been originated in animals (tremors, cramps, paralyses, contractions).

The disease generally occurs epidemically and only affects the *poorer classes of the population* as it is they alone that use lathyrus as a food. In India, the extent of poverty in a village can be gauged by the quantity of lathyrus kept for sale in the bazaars.

The disease usually sets in during the *damp and cold season.* "Colds" are regarded as a predisposing cause.

Sometimes the eating of lathyrus for one month suffices to induce the disease ; in other cases the pulse may have been eaten for several months before the illness shows itself.

Lathyrism attacks *young persons* by *predilection* and men are more often attacked than women.

The disease is also observed among animals (oxen, horses, pigs, geese). The symptoms in horses are shortness of breath (suffocation) caused by recurrent paralysis, and sudden death on exertion ; these symptoms are not observed in man.

SYMPTOMATOLOGY.

The onset of the disease is usually *sudden,* occurring frequently at night. Digestive disturbances, colicky pains and diarrhœa, which precede the outbreak, are often unheeded by the patients. Sometimes an attack of fever of moderate severity lasting from several hours to a day may precede the period of invasion. There may be also pains in the lumbar region and the legs, and weakness, tremor and stiffness of the lower extremities so that walking becomes a difficulty. Gradually the typical symptoms of *spastic spinal paralysis* develop.

The gait is then characteristic. Walking is irksome, and can only be accomplished with the help of a stick. The legs are rigidly extended, the heels do not touch the ground, the feet are slightly rotated inwards, and the toes are flexed ; at each step the body is projected forward, while simultaneously the muscles of the vertebral column on the side opposite to that of the foot advanced become strongly contracted. The patients often fall while walking and the parts of the feet dragged over the ground are chafed and rubbed into a sore. Finally walking may become quite impossible. There is no ataxia.

The *electric excitability of the muscles* of the lower limbs is almost always diminished ; the reaction of degeneration is, however, not observed (Mingazzini and Buglioni).

The arms as a rule are not involved, but sometimes there is trembling of the hands.

The sensibility of the legs does not always exhibit disturbance. Anæsthesia is sometimes observed after prior hyperæsthesia and paræsthesia (formication).

The *cutaneous reflexes* of the legs are occasionally increased or diminished ; the *tendon reflexes* on the other hand are always greatly increased and spontaneous clonic spasm appears during walking. Vasomotor disturbances are not, as a rule, present.

In regard to *trophic disturbances* it is observed that muscular atrophy sets in after the disease has persisted for some time. Hattute, &c., in a series of cases observed in Algiers, saw gangrene of the toes, of the feet and legs, caused by obstruction of the arteries, and ascribed this condition to lathyrism. Probably, however, in these cases it was a question of ergotism, which is sometimes observed in Algiers.

There is frequently retention and incontinence of urine, and impotence. There are no cerebral symptoms ascribable to lathyrism.

The patients living in want and misery are generally much emaciated.

In some cases the disease can be cured. Mostly, however, recovery is not complete, for permanent spastic symptoms and also real contractions are left behind. Lathyrism *per se* does not cause death.

PATHOLOGICAL ANATOMY.

Pathological observations up to the present are lacking. Only one *post-mortem* examination of little value has been published by Grandjean. The patient's death was caused by malarial cachexia, and Grandjean found a softening of the spinal column above the lumbar enlargement extending about 6 cm.

According to the clinical features of the disease, the conclusion must be accepted that lathyrism is a *disease* of the *lateral columns* of the spinal cord.

DIAGNOSIS.

The diagnosis of lathyrism, which, as a rule, appears epidemically, offers no difficulties. It is especially to be distinguished from *beri-beri*, with which it has been sought to connect it, by the absence of dropsy and cardiac symptoms, the spastic symptoms, the non-participation of the arms in the disease, the infrequency or absence of disturbances of sensation, the increase of the tendon reflexes, the slight changes of the electrical excitability, as well as the disturbances of micturition which are so often present at the commencement of the disease.

PROGNOSIS.

The prognosis of lathyrism is good as regards life but bad as regards complete recovery.

PROPHYLAXIS.

The prophylaxis consists simply in avoiding the lathyrus as a food.

TREATMENT.

The chief factor in treatment is the discontinuation of lathyrus as a food.

Good results have frequently followed counter-irritation in the region of the lumbar vertebræ by means of the thermo-cautery, or by painting with

a mixture of tincture of iodine and croton oil. In addition to this plan of treatment, warm baths, electricity, massage, &c., are employed, and bromide potassium (2·0—5·0 gram. daily) has been recommended.

Cystisus cajan, called in Hindostanee *urhur* or toar, very similar to the common laburnum (cystisus laburnum), is another pulse, after eating which in India poisoning is likewise observed. This pulse is eaten on account of its agreeable flavour although its poisonous qualities are well known, and in consequence of its high price only the rich classes of the people can afford it. The symptoms of poisoning by this plant consist of intestinal catarrh and skin affections, such as urticaria, bronzing and dryness of the skin, and burning of the hands and feet. In course of time the bones of the legs become painful, the periosteum becomes thickened, mental and bodily vigour suffers, and women become barren. The poison appears to be principally contained in the husks.

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III.

ATRIPLICISM.

Atriplicism, so-called by Matignon,[1] is a disease that frequently occurs in North China (Peking) and which is manifested by localised œdemas, disturbances of sensibility and vaso-motor and trophic disorders. According to Matignon this complaint is caused by poisoning with atriplex.

Atriplex littoralis, the coast orache, is a plant belonging to the family of the Chenopodiaceæ, which appears in two forms in Mongolia and North China as *atriplex angustissima* and *atriplex serrata*. The latter, called by the Chinese Lao-li-ts'ai, grows in Peking and its vicinity as a weed, in the courts, gardens, and along the walls of the houses; its tasty, delicate young shoots are often eaten by the poor people, particularly the beggars, almost raw, either in half-cooked bread dough, in a kind of pancake, or as a salad. All those that eat the plant do not fall ill presumably because some persons possess immunity, and also because all the shoots of the plant are not poisonous. It is said they are never poisonous if well washed and cooked and if the red leaves be picked out. Probably the poison is not in the plant itself, but is contained in a parasite clinging to it or in the secretion of the parasite. Frequently a small species of plant-louse of a greenish-yellow colour is found on the plant and perhaps the disease may be attributable to this parasite. Unfortunately Matignon mentions nothing further on the subject.[2] Laveran is of opinion, judging from the peculiar localisation of the affection, that the complaint is not caused by eating the plant, but comes to pass through persons plucking it with the thumb and fore-finger, the toxic material thereby getting into the fingers, and from thence being carried to the face.

Experiments conducted by Matignon to induce the disease by rubbing the shoots on the hands and face were futile, and the hospital attendants also who tore up the plants with their arms bare did not become affected. It seems, however, that in these experiments it was not ascertained if the plants in question were infested by the plant lice mentioned or not.

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[1] De l'atriplicisme (intoxication par l'arroche). China Imp. Marit. Customs Med. Reports. 54th issue. Shanghai, 1898.

[2] Mégnin calls attention to a kind of mite found in Mauritius and in the Malay Archipelago; it is called *holothyrus coccinella* (Gervais); contact with it causes local symptoms of inflammation which may be very severe, especially in the mouth and throat if the hand with which the insect has been touched is carried to the mouth (Bull. de l'Acad. de méd., 3 Sér., xxxviii., 1897, p. 187).

The disease occurs almost exclusively amongst *beggars*. In 1895, when a famine prevailed in Peking on account of the war between the Japanese and the Chinese, this disease was frequently observed.

Age exercises no influence.

The *female sex* furnishes the largest contingent of sufferers, but this is not because women have a particular susceptibility to the toxin, but it is explained by the fact that they are more exposed to the noxious influence of the plant, for the woman, as a rule, has to make shift with the scraps that the man chooses to leave her.

That the *general feebleness of the body* has a predisposing influence is revealed by the fact that the weakest persons—young or old—always are attacked.

The *onset of the disease* is *sudden*, occurring within 10 or 20 hours after the plant has been partaken of.

The *tips of the fingers*, sometimes only of the thumb and forefinger, become *cold* and are the seat of painful tingling, and the *backs of the hands* begin to *itch*. Almost simultaneously, *i.e.*, within half or three-quarters of an hour afterwards, the *backs of the hands* and the *fingers* also begin to *swell*. *Cyanosis* of the nails and finger tips sets in, the thumb and forefinger being again most affected. The œdema quickly increases and spreads over the hands and *forearms* without, however, extending beyond the elbows. The œdema does not affect the inner surface of the forearm but forms a sort of triangle, the base of which is situated at the wrist joint and the apex at the external condyle. The skin remains pale and feels cold. The swelling is as a rule accompanied by sharp pains which are increased by movement and by pressure, or when the arm hangs down. In consequence of the œdema the movements of the hand and fingers are hampered, and the fingers are flexed and separated.

Within a few hours *swelling of the face* sets in, but in rare cases the disease starts from the face. Sometimes the swelling is so considerable that the eyes are completely closed. In slight cases the swelling is confined to the eyelids and disappears again after twenty-four hours. The *nose is of a bluish colour and is cold*, often anæsthetic. The swelling of the face is attended by little or no pain, but it causes violent itching, and in consequence of the scratching ecchymoses of variable extents ensue on the face and arms.

Sometimes the œdema is confined to one side of the face and the swellings may not be symmetrical on the arms.

The sensibility is diminished on the fingers and there is sometimes complete anæsthesia of the thumb and forefinger. Sensitiveness to heat on the other hand is considerably augmented over the affected areas. Warmth and the influence of the rays of the sun increase the pain to such an extent that the sufferers are apt to shroud their faces and hands even in the hottest weather.

The general health of the patients is not disturbed, the urine never contains albumen, and the pulse is but slighty slower than normal.

The swelling mostly disappears from the face in two or three days ; it is seldom prolonged to a week. For a similar period the œdema of the hands and forearms persists, the œdema occasionally lasting on the hands for ten days.

The skin is shed in large patches on the ecchymosed areas. Sometimes, even during the first days of the illness, *blisters* varying in size from a hempseed to a hazel nut, form on the patches ; and these through becoming confluent, attain the size of a five-shilling piece containing a

more or less opaque yellow fluid ; when these blisters burst they dry up to impetigo-like eschars. In other cases, after the œdema has disappeared, the skin appears sodden over the entire area of the ecchymosed patches, and superficial and often painful *ulcerations* which easily bleed result. The ulcers may take a month or six weeks to heal ; and cicatrisation occasionally ends with the appearance of keloid-like formations, a phenomenon not uncommon amongst the Chinese. The ulcerations are often accompanied by fever the temperature rising to 38° or 39°. The tongue at the same time is furred, the appetite diminished, and the bowels costive. In some cases there is enlargement of the lymphatic glands at the elbow and in the axilla.

As a consequence of the disease, Matignon once observed dry gangrene of the last phalanges of the third and fourth fingers.

We have no *post-mortem* observations to guide us as to the exact nature of atriplicism. The seat of the disease is to be sought in the nervous system (medulla oblongata, cervical spinal cord, or peripheral nerves).

The *diagnosis* of atriplicism is not difficult. Only two diseases—Raynaud's disease and erythromelalgia—are somewhat analogous. In the differential diagnosis between *Raynaud's disease* and atriplicism it is to be noted that the former is a disease of adolescence, that it also affects the toes, that œdema is absent, and sensibility more severely deranged, the pains are increased not by warmth as in atriplicism, but by cold, and the course is slow and intermittent. In erythromelalgia the diseased parts look red but are not œdematous, the disease does not extend beyond the hand, and cyanosis, disorders of sensibility, ecchymoses and blisters are wanting.

The treatment of atriplicism consists at first in the administration of saline aperients ; later on tonics (quinine, arsenic) are given, and Matignon sometimes added disinfectants to these (benzoate of soda, benzo-naphthol, salol). Locally oil of hyoscyamus with opium and chloroform and cold compresses are applied.

IV.

LACQUER POISONING.

In China and Japan, the homes of the lacquer industry, a disease often occurs among persons that handle lacquer, such as lacquer tapsters, lacquer dealers and lacquerers ; this ailment is attributable to the injurious effects of lacquer and is called Urushi-kabure, *i.e.*, lacquer poisoning by the Japanese.

The lacquer is extracted from the lacquer tree, *Rhus vernicifera* (De Candolle), in Japanese called Urushi-no-ki, a tree belonging to the family of the Anacardiaceæ, and which attains a height of about 8 m. and a circumference of 1 m. The tree is cleft by the lacquer tapsters, and the juice that exudes, a treacle-like brown balsam which becomes black on exposure to the air, reaches the hands of the lacquerer after it has gone through various cleansing processes and received the necessary additions of colour.

The lacquer disease is originated not only through *direct contact*, but also through *evaporation of the lacquer*. The poison, whatever it is, is of an evanescent nature, for the poisonous properties disappear with the drying of the layer of lacquer. A considerable portion of the poisonous influence is removed during the process of preparing the various sorts of lacquer and the stirring of it in open vessels. Raw lacquer and its derivatives are therefore the most dangerous.

The lacquer tree itself diffuses no injurious vapours, as is proved by the fact that in Japan those people whose calling it is to cultivate lacquer trees plant them immediately in front of their houses, and only strictly forbid their children to touch the trees.

The susceptibility of individuals to the poison varies remarkably. Görtz mentions the case of a lady who became affected every time she visited a lacquer-ware warehouse in which there were newly lacquered articles.

There is no such thing as becoming used to the poison. The belief prevalent in Japan that every lacquer worker must have the disease once and thereafter is immune, is stated to be fallacious by Görtz, who repeatedly saw patients who had been attacked for the fifth and sixth time.

The usual symptoms of lacquer poisoning are as follows : A few hours after the poison has taken effect, the patient is in a slightly feverish condition and complains principally of itching and a disagreeable feeling of tension of the skin of the head, face and limbs. Soon after œdema of the affected parts of the skin sets in with catarrh of the contiguous mucous membranes (rhinitis, conjunctivitis, &c.). Small red papules rise on the œdematous skin ; they gradually increase in size and small blebs with sero-purulent contents form on their apices. On the arms the

eruption usually extends to the elbows, on the legs to the knees, and at these limits sharp lines of demarcation are perceptible. In men the scrotum and the prepuce always participate in the œdema, and in women the labia majora are similarly affected.

The congestive symptoms may be so severe in serious cases that cerebral symptoms of considerable intensity may be set up. The fever in such cases is very irregular, but the temperature does not usually exceed 39°.

The pustules, which frequently become confluent, dry up or burst and become covered with eschars, but large purulent ulcerations may result.

The disease never has a fatal termination.

In China, according to Du Halde, the workers in lacquer *prophylactically* rub their faces and hands with rape seed oil in which pork has been boiled; after work they rub in a decoction of chesnut and pine-bark, saltpetre and a kind of amaranth (Amaranthus tricolor) made with water. During work they cover the head with a linen mask, and the upper part of the body with a leathern apron. In Japan it is not customary to use any such precautions.

The treatment consists in energetic washing with soap and smart scrubbing of the skin immediately after the poison has taken effect in order to remove as much of the poison as possible. After the onset of the eruption, means should be taken to check the inflammation by such means as cold compresses, tepid baths, dressings with aqua plumbi, lime-water, or astringent decoctions of oak-bark may be used ; sponging the surface with a solution of carbolic acid is also of service.

In Japan the juice of the common garlic applied externally is used as an antidote.

Similar inflammations of the skin are set up by the juice of other kinds of rhus, more especially rhus toxicodendron (Michx.), rhus lobata (Hook), rhus venenata (de Candolle), rhus pumila (Michx.), rhus perniciosa (Kth. and others); all these plants are natives of America.

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V.

POISONING THROUGH SNAKE VENOM (OPHIDISM).

THERE are *poisonous snakes* (*Thantophidii*) in most countries of the torrid and temperate zones, but they are particularly numerous in tropical countries, as, for instance, in British India, where 20,000 persons (in 1898, 21,921) yearly fall victims to snake-bites.

Poisonous snakes are divided into two classes—the *viperines* and *colubrines*—distinguished from each other by their structure and by the qualities and toxic effect of their venom : in the former the poison fangs are pierced throughout their centre, thus forming tubes, whereas in the latter they are merely furrowed.

The most important of the vipers are : the *rattle-snake—Crotalus—* of which there are several species in North and South America; the *lance snake—Trichonocephalus lanceolatus*—Wagl. (Martinique and Santa Lucia) ; the *jararaca—Trichonocephalus jararaca pr.*—Neuwied (Brazil) ; the *mocassin* snake — *Trichonocephalus piscivorus* — Holbr. (North America); the *Trimeresurus viridis*, Merr (East Indies and China); the *puff-adder—Clotho arietans*—Gray (South-West Africa) ; the *ketten-viper— Daboia Russellii*—Wagl. (East Indies); the *echis caninata*, Wagl. (East Indies, North and Central Africa) ; and our endemic adder—*Vipera berus* —Daud.

The most important *colubrines* are : The *coralline snake—Elaps corallinus pr.*—Neuwied (Brazil and Mexico) ; the *spectacled snake—Cobra di capello naja tripudians*—Merr (East Indies); *Cleopatra's snake—Naja haje*—Merr (Africa) ; the *Crait*, or *blue adder—Bungarus cæruleus*—Daud (East Indies) ; the *black snake—Pseudechis porphyricus*—Wagl. (Australia) ; the *tiger snake—Hoplocephalus curtus*--Gthr. (Australia) ; the *spine-tailed death adder—Acantophis antarctica* (Australia) ; and the *sea-serpents*, or *hydrophidæ*, which principally live in the Indian and Pacific Oceans, and thence ascending the rivers, endangering the lives of bathers ; of these the most common is the *hydrus platurus*.

The *venom*, which is secreted from a poison gland corresponding to the parotid, situated between the temporal and masseter muscles, is a clear, colourless, yellowish or greenish liquid, which, over chloride of lime, easily dries up to a substance resembling gum arabic, but without thereby losing any of its poisonous qualities. The reaction of the venom is either acid or neutral. Its specific gravity varies exceedingly, but in most snakes it amounts on an average to about 1050.

The quantity of venom ejected depends on the size of the snake. A rattle-snake loses about 0·25—0·3 g. at every bite ; a common viper, on

the other hand, only 0·03 g. of venom. Through repeatedly biting the supply of venom becames exhausted, and is only slowly replaced.

The snake venom contains at least two *poisonous albuminoid bodies* (*toxalbumin*), of which one acts locally on the tissue of the bitten spot and its vicinity ; the other, after absorption, causes paralysis of different nerve centres, particularly the respiratory and vaso-motor centres ; it also has a paralytic effect on the myocardium and the cardiac ganglia. By being heated to 80° for ten minutes the poison, which acts locally on the tissues, can be removed without causing the paralysing effects to disappear.

The toxalbumin is contained in the venom of different species of snakes in different proportions, so that after the bite of one the local effect is less pronounced than the remote effect, and *vice versâ*. Thus the local symptoms, after poisoning with the venom of the rattle-snake and chain snake, are more pronounced than after poisoning with cobra venom. If considerable quantities of venom are inoculated, such as is the case with energetic bites of large snakes, the paralysis of the nerve centres ensues so rapidly that the local effect cannot develop at all.

The symptoms which set in after a snake-bite depend on the species, size, and strength of the snake and the quantity of venom inoculated, which may be small if the snake has been biting a short time previously. The symptoms, moreover, depend on the size, the condition of nutrition, and the bodily strength of the victim : children and badly-nourished and weakly persons run the most danger. The site of the bite has also an influence ; those parts of the body that can be seized by the snakes in their jaws, as the fingers and toes, in which the poison fangs can penetrate more deeply, are the most dangerous parts in which to be bitten.

The *symptoms* of poisoning with snake venom are two-fold—*local* and *general*. In regard to the local manifestations, the pain caused by the bite is mostly slight, like the prick of a needle. More rarely the pain is severe, continuous, and takes in a large part of the bitten limb. A swelling soon appears in the vicinity of the wound, and at times quickly spreads from the extremities to the trunk, attaining wide dimensions. Simultaneously the skin contiguous to the bitten spots assumes a livid or violet tint, while numerous ecchymoses appear. At the same time a sensation of numbness in the injured parts sets in, caused by the pressure of the infiltrated tissue on the nerves beneath, and the temperature of the part falls. The neighbouring lymphatic glands become enlarged, and phlegmonous lymphangitis and even extensive gangrene, may set in. These symptoms may be accompanied by fever, and are attributable to the fact that the serum loses its normal bactericidal quality through the effect of the venom, and on this account the tissues easily suppurate. In this manner a fatal issue may be brought about by the local disturbance only weeks after the bite.

The general or *remote symptoms* cause death far more frequently. Occasionally, when the bite has pierced a vein, death ensues in from five to fifteen minutes, or the victim may even succumb in two minutes ; in other cases death takes place in as many days. In the severest cases the persons bitten suddenly lose consciousness and become comatose, and this condition is occasionally accompanied by tetanic convulsions or delirium. In less severe cases, giddiness, headaches, congestion of the face, a sensation of fatigue and general depression, sleepiness, a sense of terror, restlessness, and dyspnœa set in. The features become pinched, the limbs become cold, and a cold, clammy sweat breaks out. The pulse is small and irregular, at first accelerated, but later on is retarded. Respiration also, after at first being rapid, becomes slow and superficial. With these changes there is nausea, vomiting, diarrhœa, profuse salivation,

thirst, gastric and abdominal pains, and the urinary secretion is generally quite suppressed. Transient loss of consciousness, or coma and convulsions, especially in children, may set in. Sometimes symptoms of paralysis are manifested, the power of speech and capability of swallowing being arrested. The pupils are sometimes dilated and fixed (after the bites of the rattle-snake, Indian vipers and the poisonous Australian snakes); sometimes, on the other hand, they are contracted, but react to light (after the bite of the cobra). Sometimes, particularly after bites of the Indian vipers, a hæmorrhagic tendency developes, and petechiæ, bleeding of the nose, spitting of blood, vomiting of blood, bloody stools, &c., set in. Occasionally, also, icterus and multiple abscesses are observed.

Death, which seldom occurs before from six to twelve hours after the bite of even the most dangerous venomous snakes, is caused by respiratory paralysis. Nevertheless, it is impossible to prolong life by artificial respiration, as the venom simultaneously has caused paralysis of the heart.

Should the condition tend to a favourable issue the patients often recuperate wonderfully quickly. Occasionally recovery is slow, extending over weeks and even months. After bites of the Indian vipers albuminuria is observed during convalescence. In isolated cases disturbances remain for several years, or may persist during life. The disturbances referred to consist in frequent attacks of pain, swelling, &c., of the bitten spot, with gastric disorders, and these symptoms are repeated every year at the period of the year the injury was inflicted. Much more rarely the patients develop an exquisite cachexia.

The *anatomical* changes found in persons that have died of snake-bite are trifling. The tissues in the vicinity of the bite are permeated by œdema and hæmorrhages, and the vessels are distended. The blood is sometimes liquid, sometimes more or less coagulated. Hæmorrhages are found in the most diverse organs, particularly after the bites of vipers. The cerebral meninges are often hyperæmic, and the cerebral ventricles filled with opaque fluid. In other cases, on the contrary, there is anæmia of the contents of the cranial cavity. The lungs are generally hyperæmic, the mucous membrane of the bronchi injected. The kidneys are sometimes normal, and sometimes exhibit extensive hyperæmia ; the latter being particularly the case after the bites of vipers.

Microscopically Nowak found fatty degeneration in the *liver* and *kidneys,* and rapid necrosis of the hepatic cells and renal epithelia, as also a few small round-cell infiltrations along the bile ducts. Probably these organs try to excrete the venom and thereby become affected.

The *diagnosis* of snake-bite seldom offers any difficulty, being founded on the statements of the patient or his companions. The snake is often killed and brought with the sufferer to substantiate the statement, which is, moreover, confirmed by the evidence of the bite. At the place bitten two small wounds are seen, having the appearance of pricks by a needle, and bleed but little if at all. They can mostly be seen with the naked eye, but occasionally can only be recognised by means of a magnifying glass.

The *prognosis* largely depends on the kind of snake. The bites of the venomous snakes of India (chain viper, echis caninata, hooded cobra, Crait snake, and the sea snakes) are accounted as almost certainly fatal if the snakes are of large size and immediate help is not at hand. Of those bitten by venomous snakes, 25—35 per cent. die in India, 25 per cent. in America, and 7 per cent. in Australia.

Treatment has a twofold purpose : (1) *To prevent the absorption of the venom ;* and (2) *to remove the venom from the bitten place, or to render it abortive locally.*

The first thing to do to prevent the venom being absorbed is to apply a ligature close above the wound, sufficiently tight to arrest the flow of blood in the blood vessels. For this purpose anything at hand is taken —a belt, a twisted cloth, a thong, an india-rubber cord, &c.—and tied firmly around the limb above the seat of the bite ; the ligature is then tightened by passing a stick under it, and twisting it so as to form an improvised tourniquet. Should the bite be situated on any part of the body where a ligature cannot be applied, as on the face, the place must be immediately cut out. If it be on a finger or toe, and caused by a large serpent, it is advisable to at once amputate the member.

After applying the ligature, one should make an incision over the bite, and try to get rid of the venom by sucking or squeezing the wound. Sucking is done with the mouth, or better still with a dry cupping glass, if one is handy. Sucking with the mouth requires the greatest care. It must only be attempted if the lips and mucous membranes of the mouth are free from cracks or injuries and, when it is the question of large quantities of venom, the process as Fayrer demonstrates is not free from danger, as snake poison may be absorbed by the mucous membranes (conjunctiva, stomach) as well as by the serous membranes.

The next process is to at once destroy the poison, and this is done either by *red heat* (thermo-cautery, galvano-cautery) or by chemical agencies. Of chemical agencies, corrosives come first, and according to Husemann, *caustic potash, liquor antimonii chloridi*, and *chromic acid*, used pure, are the most reliable. A simple but effective process of cauterisation is used by hunters, it consists in washing the wound, sprinkling gunpowder on it, and setting it alight.

Besides these, the remedies which have been recommended as *antidotes with local effects* are very numerous, but three only have stood the test of critical experimental proof; these are *permanganate of potash, chloride of gold*, and, above all, *chloride of lime*. Next to the ligature they constitute the most efficacious treatment in the case of snake-bite. Permanganate of potash, which was introduced as a means of treatment by Lacerda, is used in a 3 or 5 per cent. solution, chloride of gold in 1 per cent. solution, and chloride of lime in 2 per cent. solution ; of these 8—10 ccm. are to be injected into the wound and its vicinity. Chloride of lime must be prepared fresh and filtered. It is therefore advisable always to have a strong solution (about 1:10) ready, and to dilute it before use to the strength required with boiling water.

The so-called *snake stones* which are much used in India, and which consist of bezoar stones (concretions from the stomach of various animals) of artificial products from burned hartshorn, &c., have proved useless. They are laid on the wound, and their use would seem to arise from their power of absorption.

After the poison has been destroyed at the spot bitten the ligature is removed, and the further treatment of the wound is antiseptic. Threatening collapse may be averted by giving *stimulants* (alcohol, ether, camphor). Alcohol is especially indicated, and the patient should be given alcohol in quantity short of inducing a condition of inebriation. Mulled wines are recommended, or punch or grog, these being useful as exciting *diaphoresis* and *diuresis*, thus assisting the elimination of the venom absorbed. In order to assist the diaphoresis the patient should have a hot bath and be put to bed and covered with warm blankets.

As the poison is excreted through the mucous membranes of the stomach, Sir Lauder Brunton and Alt recommend *washing out of the stomach* with alcohol (brandy).

Ammonia and *strychnine* are also used as stimulants ; the former is

especially recommended by Halford and the latter by Müller. Ammonia is injected intravenously and strychnine subcutaneously.

In other particulars the treatment is symptomatic ; under some conditions narcotics would seem to be indicated.

Recently favourable results have been achieved by *serum therapy*, of which Phisalix and Bertrand, Calmette and Fraser, are the pioneers.

The " antivenene," which is prepared by Calmette in the Pasteur Institute in Lisle,[1] is derived from horses or asses that have been immunised by gradually increased doses of snake venom from various snakes (such doses being at first mixed with chloride of lime). According to Calmette, his preparation protects from intoxication and death if administered within two hours after the bite, and its effect is most efficacious when injected intravenously.

If kept cool and protected from light it retains its effect for over a year. The dose needed for a man averages 10 to 20 ccm. In serious cases it is as well to increase the dose to 30 or 40 ccm.

Calmette, however, himself desires that, even with serum therapy at hand, ligature and cauterisation, or chloride of lime, should not be neglected.

The effect of the serum, according to Calmette, does not depend on an antitoxin contained therein, but on the circumstance that the cells, more particularly the leucocytes, which provide for the disintegration of the venom in the body, become impregnated with the serum, and are thus better qualified to neutralise the venom.

According to Fraser, the ingestion of snake venom likewise generates immunity ; but Elliott was not able, experimentally, to confirm this observation.

Bile, more particularly the bile of venomous snakes, possesses an antidotal effect against snake venom (Phisalix, Fraser). Perhaps at some future period an antidote prepared from bile may be of therapeutic value.

As to *prophylaxis*, the first indication is the extermination of venomous snakes by paying a premium for each one killed ; but this method has resulted in India in the breeding of snakes. The next method is the cultivation of waste territories which, like the jungles of India, are the principal resorts of snakes.

In order to prevent the frequent intrusion of snakes into dwellings in India, Fayrer advises that the walls of houses be smeared with carbolic acid, which acts as a powerful poison to snakes, and to the smell of which they have a great antipathy. On hunting and other expeditions one should protect oneself against snake-bites by wearing high boots or gaiters. Some snakes, however, bite through the thickest leather ; and some spring up to bite and may even wound the face. When camping in the open the greatest care must be exercised.

It is most important when coming across a snake not to lose one's presence of mind. Such simple methods as warding the creature off with a stick, holding out a hat or throwing a handkerchief, sometimes suffice to ward off the danger. Moreover, no venomous snake, as a rule, is in the habit of attacking man spontaneously, only defending itself against accidental or intentional injuries, such as being trodden on, lain on, &c.

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VI.

AFFECTIONS CAUSED BY OTHER VENOMOUS CREATURES.

THE temperate zone, with the exception of venomous snakes, does not lack poisonous creatures, but the disturbances caused by such insects as bees, wasps, hornets, ants, gnats, stinging flies, gad-flies, fleas and bugs are but slight. Conditions are different with various venomous creatures of warm countries, the sting or bite of which may occasionally cause death, though doubtless in some cases the danger is exaggerated.

(1) **Scolopendra** (Centipedes).—The scolopendra belong to the class of *myriapods* or *millepedes*. They are provided with a poison gland apparatus at the base of the mandibles, from which a clear or slightly opaque, acid-reacting venom is secreted. Their *bite* is recognisable by two minute specks of blood. The scolopendra are nocturnal in habit; they lie secreted during the day and seek their prey by night.

The European species do no harm, whereas the tropical kinds, such as the *Scolopendra gigantea*, Lin., of the East Indies, may be 20 cm. in length or even longer, and inflict painful wounds which are followed by severe symptoms. Local inflammation is set up at the spot that has been bitten and this may lead to gangrene. Should the bite be situated on the tongue or in the mouth suffocation may ensue from the swelling. The local symptoms are occasionally accompanied by general symptoms, such as vomiting, palpitation of the heart, acceleration of the pulse, oppression, a sense of terror, pains in the head and limbs, dizziness, convulsions, and, in rare cases, particularly in children, death ensues.

The *treatment* of centipede bites consists in washing and dressing them with diluted ammonia (liq. ammonii caustici 1 : 5—10 water), the application of cold (ice, goulard water), and, if necessary, the administration of narcotics.

(2) **Scorpions.** — Scorpions, which are widely distributed in the tropics, belong to the class of *arachnoidæ*, or *spider-like* animals. They possess a sting and a poison gland, situated at the end of the narrow posterior division of the abdomen. The venom is of an acid character, and is apt to be particularly strong in summer.

Scorpions generally live in dark and cool places, under stones, in cellars, or on ground floors. They leave their hiding-places at night, and it is when one treads on them in the dark that one gets stung.

The sting of the *euscorpius europæus*, Lin., which is a native of Southern Europe and Italy, is not more serious than the stings of bees and wasps. The various exotic scorpions are far more dangerous, and they are distinguished by their remarkable size, measuring at times 16 cm.

in length; such are *androctonus funestus*, Ehrenb. (North and Central Africa), *buthus afer*, Lin. (Africa, East Indies), *buthus occitanus*, Amour (Italy, Greece, Spain, Northern Africa). There is a species of scorpion in Durango in Mexico which, according to Cavarroz, kills 200 to 250 children yearly in a population of 15,000 souls.

The disorders caused by scorpions are partly local, partly general. The local symptoms consist of severe pains, œdema, lymphangitis, adenitis, and gangrene. The general symptoms are vomiting, diarrhœa, icterus, acceleration of the pulse and respiration, terror, oppression, restlessness, fever, decrease of strength, swoons, paralysis of the peripheral nerves, convulsions, delirium, coma, and sometimes within twenty-four to thirty-six hours death occurs. Sometimes, also, tetanus is observed, but this is probably attributable less to the scorpion venom than to an infection of the wound with tetanus bacilli. A peculiar symptom mentioned by Dalange and Guyon (Algiers), as occurring after scorpion stings, is violent erection of the penis. Posada-Arango (Columbia) states that immediately after the injury has been inflicted a sensation of numbness and heaviness of the tongue, a kind of complete paralysis of the lingual and hypoglossal nerves, set in.

The rational treatment for scorpion stings is to apply a ligature above the spot stung, which should be incised and sucked. It should then be washed, and compresses of diluted ammonia should be applied. Stimulants (alcohol, camphor, ether) should be given. Calmette's antivenene (see above, p. 337) is said to be effective also in scorpion venom.

(3) **Spiders.**—These belong to the same class as the scorpions. The spiders bite with the claw-like maxillary feelers, which are hollow, and lead to the poison glands in the terminal articulation of the feelers. The venom of spiders is likewise very acid.

The following spiders deserve mention : The *Minier spider* of Costa Rica—*Arana picacaballo ;* a kind of mygale spider found in Italy, France, Switzerland, and rarely in Germany (Bingen)—*chiracanthium nutrix*, Walck; the common *malmignatte—Theridium tredecim guttatus F.*—which is found in Italy, Corsica, and Sardinia ; the *karakurte* of the Kirgise Steppes—*Latrodectes lugubris* (Matschulski), which is particularly dangerous to camels, horses, and cattle ; the native *tarantula—Tarantula apulica* (Rossi), of Italy, Spain and Portugal; the *Russian tarantula—Lycosa singoriensis* (Laxmann) (South Russia) ; the *Andalusian poison spider—Cteniza sarmentaria*, Lin. ; and the *katipo* of New Zealand.

The symptoms arising from the bites of spiders resemble those arising from scorpion stings. There are local symptoms of inflammation, which are mostly manifested by the appearance of vesicles ; occasionally, however, in spite of severe pains at the site of the wounds, which may spread thence more or less over the entire body, local inflammation may be but slight or even entirely absent. Sometimes nausea, vomiting, thirst, dyspnœa, oppression, anxiety, restlessness, great weakness, coldness of the extremities, headaches, and occasionally even convulsions set in. After the bite of the karakurte a typhoid condition has been observed to develop, and death ensues in two or three days. Sometimes extreme prostration remains for weeks. As a rule, however, the course is favourable, the symptoms disappearing after a short time.

The treatment is similar to that for scorpion stings, the severe pains sometimes necessitating the use of narcotics.

(4) **Ticks.**—Even the tiny ticks of the *Argas* family, which also belong to the arachnoids, possess a venom by means of which they may become very troublesome to man.

The Persian poison bug, Argas Persicus (Fischer), which is also found in Egypt, lives in cracks in the ground and walls of old houses, crawls over people at night, in the same manner as our bugs, and when sucking blood they inject some venom into the wound, causing severe pain followed by violent itching. These bugs may become such a plague that all the inmates may be driven from their villages by them.

Sometimes more serious disturbances follow the bite of this venomous bug. In Miana, North Persia, a peculiar disease attributed to its bite occurs. It is attended by severe pains, delirium, convulsions, and remittent fever, and sometimes even causes death. Natives of the country possess a relative immunity, and this fact is considered to be owing to their having been bitten before and recovered from the illness.

Along the Zambesi and its tributaries there is another kind of tick, *Argas moubata* (Murray), which likewise inhabits old houses ; by day it hides in the crevices of the floor and walls, coming out at night to seek food, when it attacks animals as well as human beings. After its bite, pain and irritation are set up at the place bitten, which gradually spread to the abdomen, to be followed by vomiting and stools containing blood with or without fever. The illness lasts a few days or weeks, and in some cases has a fatal issue.

The bites of two kinds of ticks, one a native of Central America and Texas—*argas talaje* (Guérin-Méneville), and the other a native of Mexico—*argas turicata* (A. Dugès), are likewise supposed to cause serious disturbances.

In all these cases, however, it is probably not the effect of the venom of the ticks in question that induces the disease, but effects caused by parasites, of which the ticks are hosts, and which are transmitted with the bite. This is the case with another kind of tick, the *ixodes bovis*, and the Texas fever of cattle.

The *treatment* of disorders caused by ticks is merely symptomatic.

It is advisable, as a *prophylactic*, to fumigate houses infested with ticks with sulphur, to pour boiling water, petroleum, or benzine into the crevices, and to use insect powder. If ticks are found stuck fast to the skin they should not be torn off, as their proboscis is easily separated, and would remain embedded in the skin. The application of a drop of olive oil, turpentine, benzine or petroleum will cause them to loosen their hold.

(5) **Fish.**—Several families of fish, belonging to the order of *acanthopteri*, possess prickles on their fins having connection with a poison gland apparatus by which they can convey poison through a puncture which may even cause death. The accident may occur when engaged in fishing, bathing, or even when preparing fish for table. Examples of such fish are : the *scorpæna scropha* of the Mediterannean Sea ; *trachinus vipera* (Cuv. et Val) found in European waters ; the John Dory—*trachinus draco* (Cuv. et Val) found on the coasts of Europe and the West Coast of Africa ; *synanceia brachio* (Lacep), East Indian Ocean and Polynesia ; and *pelor japonicum* (Cuv. et Val) Japan.

The stings or punctures from such fish induce local symptoms, of which the most frequent are symptoms of inflammation accompanied by fever, severe pains, much swelling, lymphangitis, and lymphadenitis ; gangrene may also arise, but this is in all probability contributed to by bacterial influences. There may be besides symptoms of general poisoning, such as nausea, vomiting, diarrhœa, precordial anguish, delirium, convulsions, cold sweats, swoons, &c. I attended a Japanese in Kioto who had had a sting from a *pelor japonicum* on the left thumb. Phlegmonous and gangrenous symptoms rapidly spread to the arm, necessitating the amputation of the forearm eleven days after the injury had been inflicted.

Other fish poison by their *bite*, being provided with poison teeth on their palates. Such are the *conger eel—Murœna helena*, Lin., found in the Mediterranean Sea, near Madeira, and in Australian waters ; *stomias boa*, Risso (Mediterranean Sea) ; and *tetrodon fluviatilis* (Indo-China).

The treatment of injuries caused by such fish consists in incision, pressing and sucking the wound, cauterisation with ammonia, nitric acid or hydrochloric acid, and the administration of stimulants.

Various fish of the family of *tetrodon, diodon, barbus*, and *meletta* harbour a poisonous material, to *partake* of which would be *injurious*. Their *spawn* in particular is poisonous, and other organs in a less degree ; the flesh itself is, however, innocuous. The poison is not destroyed even if boiled for hours, and people have been known to have been killed by it.

Poisoning by *tetrodon* is well known, especially in Japan, where there are several species ; they are called *fugu* by the Japanese, and are often used for suicidal purposes. The symptoms set in three to fifteen minutes after eating the fish, and consist of an unpleasant sensation in the region of the stomach, abdominal pains, burning in the fauces, nausea, severe headache, collapse and fainting ; death may occur in a few hours from paralysis of the respiratory muscles and heart.

Diodon sets up similar symptoms. The constitutional effects induced by *barbus* resemble cholera nostras. *Meletta* causes severe gastro-enteritis, with symptoms of paralysis and convulsions. A fatal issue may likewise result from these poisons.

The *treatment* consists in immediately emptying the stomach of its contents by means of emetics or the stomach pump. Stimulants, artificial respiration, faradisation of the diaphragm, should also be tried. Goertz saw good results in one case (tetrodon) from subcutaneous injection of strychnine (0.002).

In conclusion, the following remain to be mentioned :—

The Rat-bite disease has recently been reported by Miyake from Japan, and according to whom it occurs frequently on the four principal islands, Hondu, Shikoku, Kiushiu, and Yesso.

Miyake states that the bite of the rat sets up a peculiar ailment characterised by symptoms resembling intermittent fever, accompanied by a reddish-blue exanthem and nervous symptoms.

The construction of Japanese dwellings, being mostly of wood, allows rats to house in them, and in consequence it frequently occurs that people are bitten by these animals during sleep or when engaged in their capture. The bites are frequently, but not invariably, followed by the disease, the genesis of which is explained in various ways. According to one opinion there is a certain venomous rat among the family of rats, the bite of which causes the disease. Miyake, on the other hand, is of opinion that it is a question of illness in rats suffering from a disease analogous to rabies in dogs. Perhaps a specific bacterium in the sputum of the mad rats is the cause of rat-bite disease, although hitherto nobody has as yet met with a diseased rat of the kind.

Once the affection was observed after a bite from a *weasel*, an animal which is itself a destroyer of rats, and therefore might easily acquire the venom from a rat whilst catching it.

Sex and *age* exercise no influence on the development of the disease, but *individual predisposition* seems to play an important part in the etiology.

Certain foods, chill, and bodily hardships are given as determining *causes*.

The *period of incubation* is said to be remarkably diverse, and may

fluctuate between a few hours and several years. (?) In the majority of cases, however, it lasts between one and three weeks.

The onset of the actual disease is preceded by indefinable *prodromal symptoms* which last a day or two.

Mostly, however, the onset is sudden, commencing with fever that sets in with a slight rigor and rapidly rises. There is also an inflammatory reaction at the seat of the wound which has already healed. The part bitten swells, becomes indurated, assumes a bluish-red colour, and becomes more or less painful. During the further course vesicles form on it or the spot becomes gangrenous. In rare cases there may be a total necrosis of the affected part, as, for instance, of a finger or toe. The neighbouring lymphatic glands swell and lymphangitis frequently develops.

The *fever* is of a characteristic intermittent type, attacks of fever of two or, more rarely, of three days' duration alternating with afebrile intervals of three or four days, or more rarely of two, five or six days. The height of the fever varies between $38.5°$ and 40—$41°$. The pulse averages 110—120 beats per minute.

General languor, pains in the limbs, rheumatoid muscular pains, heaviness of the head, headaches, dizziness, singing in the ears, photophobia, darkening of the field of vision, precordial agony, secretion of sweat, loss of appetite, thirst, nausea, and occasionally diarrhœa or constipation, and in rare cases delirium and coma, are all symptoms that may set in with the fever.

The patient soon becomes weakened, the face looks pinched, the complexion cachectic, and slight œdema appears on the face, hands and feet. Icterus has never, hitherto, been observed. The liver and spleen are not enlarged, but sometimes albumen and casts are found in the urine.

Increase or loss of the patellar tendon reflexes is frequently exhibited, and sensory (paræsthesia, anæsthesia) and motor disturbances (paresis), particularly at the extremities, occur.

The characteristic feature of the disease is a peculiar *erythematous* or *papular exanthem* on the face, neck, trunk and limbs. It consists of reddish-blue, flat or raised, spots (reminiscent of erythema exsudativum), varying in size from a pea to the palm of the hand. The exanthem appears usually with the first attack of fever, but sometimes only sets in with the third or fourth attack, or even later. The rash lasts three or four days, and disappears with the fever, to break out again when the fever recurs. Towards the end of the disease, moreover, an irritative urticaria is set up.

The disease mostly ends in recovery. Of thirty-eight cases recorded by Miyake four died $= 10.5$ per cent. Death usually takes place in consequence of collapse.

A bluish-red colouring is left behind at the bite after recovery, which remains for several months or even a year.

The *duration* of the disease averages four or five weeks ; in serious cases it lasts two or three months ; but cases occur which extend for over a year.

The rat-bite disease may occur under so many different aspects that it is rational to divide them into different forms, Miyake differentiates three forms :—
(1) *The febrile form with an exanthem.*
(2) *The afebrile form with predominating nervous symptoms.*
(3) *The abortive form.*
The first is the most frequent and most important and is always accompanied with fever and an exanthem.
The afebrile form with predominating nervous symptoms is again divided into an *acute* and a *sub-acute* sub-variety. The *acute* form occurs very rarely and runs a rapid

course similar to one of the worst forms of ptomaine poison or snake bite. The victim first becomes aware of more or less severe pain on the seat of the bite. After a short time death occurs with symptoms of precordial anxiety, languor, giddiness, severe headache, dyspnœa, a remarkably small pulse, cold limbs, delirium, sensory and motor paralysis particularly of the extremities, and increasing collapse, but without the appearance of an exanthem.

The *sub-acute form* has a milder and less alarming course and may last for months or longer.

In the *abortive form* there are one or two attacks of fever with more or less pronounced general and nervous symptoms and an exanthem. The course compared to that of the other forms is very much shorter and the patients recover rapidly.

As regards the *pathological anatomy* of rat-bite disease only one case hitherto has been examined *post mortem*. In this case there was increase of the cerebro-spinal fluid and hyperæmia of the pia mater of the spinal cord ; otherwise, macroscopically there was no specific change in the organs.

The *diagnosis* of the disease, supported by the presence of a wound from a rat-bite, is founded on the three cardinal symptoms : intermittent fever, the bluish-red exanthem, and muscular pains.

The *prognosis* is according to the severity of the disease.

The *prophylaxis* of rat-bite disease consists in sucking every rat-bite, and applying a corrosive cauterisation, thorough disinfection with carbolic acid or sublimate, or even excision.

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VII.

KUBISAGARI.

Kubisagari (*i.e.*, one who hangs his head) is the name of a disease which is endemic in a certain district of the Aomori- and Iwate-Ken in the north east of the principal Island of Japan. According to Miura the disease is manifested by attacks of dimness of sight, diplopia, paresis of the cervical muscles in consequence of which the head drops (hence the designation); owing to paresis of the muscles of the trunk and extremities, of the tongue and more rarely of the lips, and of the masseters and muscles of deglutition, patients are unable to stand and walk properly, and talking, mastication and swallowing are difficult. The following symptoms, though not so constant, are often present: depression; increase of the nasal, lachrymal, and, perhaps also salivary, secretions; increase of the patellar tendon reflexes.

Miura has compiled the following scale of the frequency of the various symptoms from 63 cases observed by him:—

Dimness of vision	...	...	...	40 times.
Ptosis			...	38 ,,
Paresis of the cervical muscles...			...	34 ,,
Diplopia			...	29 ,,
Paresis of the upper limbs		...	...	26 ,,
,, ,, lower limbs		...	...	24 ,,
,, ,, muscles of the trunk			...	18 ,,
,, ,, tongue			...	16 ,,
,, ,, masseters		..	...	12 ,,
,, ,, lips			...	11 ,,
,, ,, muscles of deglutition ...				5 ,,

The muscles react to light and accommodation. The movement of the eyes is not disturbed. Miura found the double images always decussated and parallel, indicative of a paresis of the internal ocular recti muscles, and opthalmoscopically he almost invariably found hyperæmia of the papillæ and their vicinity.

The *attacks* may last from a few minutes to several hours, and may come on in varying frequency, sometimes several times in one day. The attacks may be produced by bodily exertion, particularly in a bent position when the stomach is empty, by trying the eyes, by hunger, or by indigestible food.

The *intervals* may be free from symptoms, or occasionally slight ptosis, a certain weakness of the cervical muscles, and increase of the tendon reflexes may persist.

The disease may last for many years, but never has a fatal issue.

The disorder mostly sets in *during the warm season* (May to October). It disappears during the winter only to come on again in the spring.

It is mostly observed amongst the peasants in villages, and but rarely in towns, and then only in persons who, although coming to town, are largely engaged in agriculture.

Sex and age exercise no influence, and *house epidemics* frequently occur.

The districts in which kubisagari rages are the most notorious regions in Japan for *horse and cattle plague*, and Miura considers the disease has some connection therewith. The peasants dwell under the same roof as their cattle, so that their dwellings are directly connected with the stables and are exposed to their effluvium. It is to the effects of this effluvium that Miura attributes kubisagari; and he identifies it with a disease that occurs in French Switzerland, especially in the Canton of Geneva, which was first described by Gerlier in 1886 under the designation of *vertigo paralysant*, or *ptosique* (Gerlier's disease). The inhabitants of Geneva call this complaint *tourniquet*, and Miura states that its etiology is the same as that of kubisagari.

As regards treatment, Miura in a few cases attained favourable results from the exhibition of iodide of potassium and arsenic.

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III.—DISEASES CAUSED BY ANIMAL PARASITES.

I.

THE DISEASE OF DISTOMUM PULMONALE.

HISTORY.

In 1880 Bälz discovered and described a form of hæmoptysis occurring in Japan, in which peculiar formations of a parasitic nature occurred in the expectoration. As Bälz at first erroneously mistook the parasites for psorosperm-cysts, and as psorospermiæ are a stage of development of the gregarines, he called the disease *gregarinosis pulmonum*. Leuckart, to whom the questionable objects in original preparations and drawing had been sent by Bälz as well as by myself (I having in the same year observed the first cases of this disease in Japan), recognised in them the ova of a distomum. Independently of our observations in Japan, Manson had become acquainted with the disease in Amoy, in a Chinaman, who for a long time had lived in North Formosa; Manson reported upon this discovery in 1881.

The parasite itself had been accidentally discovered by Ringer in Formosa, in the lungs of a Portuguese who died from the bursting of an aortic aneurism into the pericardium, and whose autopsy Ringer was making. Cobbold, out of compliment to the discoverer, called the parasite "*distomum Ringeri.*" The actual seat of the parasite could not be more accurately ascertained in this case, but the hiatus was supplied by Bälz through the publication of his autopsy report in 1883, and on the strength of which the worm has been designated *distomum pulmonale*.

The publications of Otani and Yamagiwa, who found the parasite and its ova in the brain, mark still further progress in our knowledge of this disease.

GEOGRAPHICAL DISTRIBUTION.

Hitherto Japan, North Formosa and Corea, are known as the geographical region of distribution of disease due to the distomum pulmonale. Stiles has lately also observed a case in North America, and Naunyn saw a case in Strasburg in a colonist who had lived in Mexico and California for fifteen years.[1] Its region of distribution is probably wide. Perhaps the hæmoptysis so common in Foochow[2] and North China,[3] is due to the presence of the ova of this parasite, and has no connection with tuberculosis. Manson did not observe the disease in Amoy except in the one case noted.

In Japan, according to Yamagiwa, the disease is distributed on the principal island — Honshu in the provinces of Awomori, Sendai, Izu, Shinano, Gifoo, Shimani and Yamagutsi; on Kiushiu in the provinces of Kumamoto, Nagasaki, Okayama, Kagoshima, and particularly prevalent

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[1] *Deutsch Med. Woch.*, 1897, Vereins Beil, No. 20, p. 146.
[2] *Amer. Jour. of Med. Science*, 1883, April, p. 547.
[3] Schofield. *The Lancet*, 1882, December 9.

in Okayama and Kumamoto. In a few of the villages it is said that nearly all the inhabitants are affected by the distomum pulmonale. The affected districts in the above provinces are all situated in mountainous regions.

Maxwell (*Journal of Tropical Medicine*, December, 1899, p. 116) published a case of parasitic hæmoptysis from Chang-poo (China). The ova described by him, however, are smaller (28—32 μ : 20 μ) than those of distomum pulmonale, and have a different appearance.

NATURAL HISTORY.

The distomum pulmonale (see figs. 30 and 31) is, according to Leuckart, a thick and plump worm, 8—10 mm. in length and 4—6 mm. in breadth, of a brownish-red colour and oval shape. It is rounded at the extremities, usually a little smaller posteriorly and quite circular on transverse section.
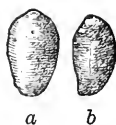
FIG. 30.—*Distomum pul-monale*, natural size. After Leuckart. *a*, Dorsal position ; *b*, profile.
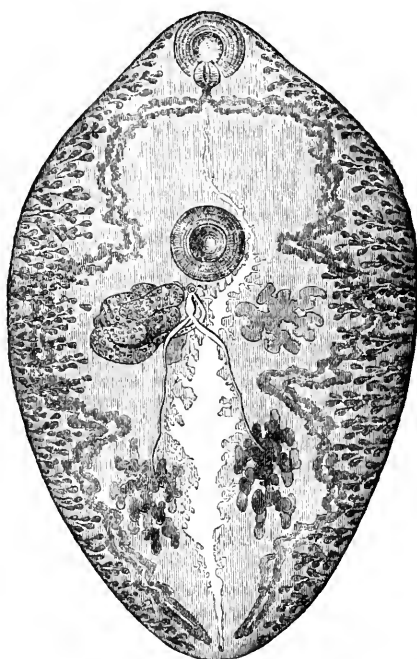
FIG. 31.—Enlarged 10-fold (dorsal position). After Leuckart.

The suckers are small and not prominent, the anterior sucker is almost ventral, and the posterior, which is somewhat larger, is at a slight distance from the centre of the body. The sexual orifice common to the male and female organs lies close behind the posterior sucker. The internal structure of the worms exhibits no essential diversity from that of other distoma.

The *ova* (see fig. 32) are of an oval shape and possess a brown, relatively thin shell, the top of which is often provided with a lid. Three to five round colourless lumps of protoplasm lie in the shell, and if the shell is burst by pressure on the cover glass the contents escape. The

length of the ova is given by Bälz as 0·08—0·1 mm. and the breadth as
0·05 mm. I found them somewhat smaller, on an average 0·061 mm.
long and 0·012 mm. broad.

Manson and Nakahama succeeded in developing the *embryos* in from
four to eight weeks at a temperature of 27—34°. They are of oval shape,
ciliated on all sides, and they are in front provided with a basilar process.

The further fate of these embryos is still unknown. All analogies
contradict the assumption that they migrate direct into the ultimate
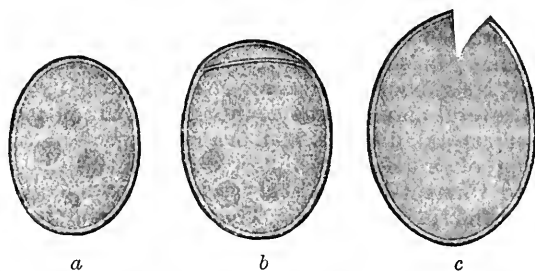
Fig. 32.—Ova of the *distomum pulmonale* from the expectoration. Zeiss' Obj. F.,
Oc. I. *a*, Without lid ; *b*, with lid ; *c*, burst empty shell.

host. They probably at first are taken up by an intermediate host,
perhaps a fish, a freshwater snail or a mussel, in which the immature
distoma are propagated and by some means or other finally reach their
destination, man. According to Leuckart it is doubtful if they imme-
diately reach the lung. The most probable conjecture is that they only
get to the lung as a part of a general infection.

Distomum pulmonale occurs in animals as well as in human beings. The worm,
according to Leuckart, is identical with the *distomum Westermanni* discovered by
Kerbert in the lungs of two tigers who died respectively in the Zoological Gardens of
Amsterdam and Hamburg. The distoma were found in the interior of fairly thick
corneous capsules. In Japan the worms have been repeatedly observed in the lungs of
pigs and dogs [free in the smaller bronchi[1]], and Ward[2] recently found them in the
lungs of a cat in Michigan, America, and in the lung of a sheep dog in Ohio ; the
American specimens were larger than those of Asia.

ETIOLOGY.

The diseases caused by distomum pulmonale occur principally in the
male sex—in youths and men in the prime of life. Old men, children and
women are rarely attacked. My patients were all strong, healthy males
between 14 and 41 years of age ; according to Yamagiwa, intemperance
appears to afford a predisposition.

We are ignorant of the manner and method of the infection, as we
do not as yet know the history of the development of the distomum
pulmonale. Probably the parasite in an encysted adolescent form is taken
into the body together with its host through impure drinking water, or
through foods eaten raw, such as fish, snails, vegetables, &c.

[1] J. L. Janson. *Mitt. der deutsch. Gesellsch. für Natur-u. Völkerk. Ostasiens.* v.,
1892, p. 349.

[2] *Cbl. f. Bakteriol u. Parasitenk.* 1894, Nos. 10, 11, p. 362 ; 1895, Nos. 9, 10.
p. 304.

PATHOLOGICAL ANATOMY.

The *lung* is by predilection the seat of distomum pulmonale. The parasites are there found either free in the *smaller bronchi* or in *cyst-like cavities* which are apt to be situated at the periphery of the organ, like hæmorrhagic infarcts. These cavities are of different sizes, but as a rule attain the size of a hazel nut; they are surrounded by a firm wall of variable thickness consisting of a neoplasmic connective tissue, with round-cell infiltrations and coiling of the vessels in the vicinity.

They communicate with the lumen of the bronchi by means of fine, sieve-like openings; in some instances they appear as sac-like diverticula of the bronchi. Neighbouring cysts are often connected with each other by channels, and several may become confluent through atrophy of the septa. Besides one or several distoma and ova, they contain a pulpy, reddish mass consisting of mucus, blood-corpuscles, disintegrated elements of lung-tissue, and Charcot-Leyden's crystals. Occasionally no worms but ova only are found in the cysts. The bronchi and lung-tissue in the vicinity of the cysts are hyperæmic, and over the cysts the lung is adherent to the thoracic wall or the diaphragm, and the diaphragm to the liver.

In the *brain* also the distomum pulmonale occurs. Otani, in one case, found the worm in *cysts* similar to those in the lung, which was likewise affected.

The right anterior lobe of the brain exhibited a tumour larger than a hen's egg, which consisted of numerous communicating cysts of sizes varying from a grain of rice to a pigeon's egg. They contained a fairly thick liquid varying from a yellowish to a darkish brown colour, and were possessed of a wall of proliferated connective tissue, having a brownish inner surface. There were, moreover, in the right posterior lobe, two large and several small cysts in which a distomum was met with, and yet another lay in the neighbouring seemingly healthy tissue. The contents of the cysts consisted of numerous ova, Charcot-Leyden's and hæmatoïdin crystal. The meninges were thickened over the cysts; they were opaque, and adherent to the brain substance.

In one case Yamagiwa found ova in the cerebral centres. Their presence there was undoubtedly due to embolism.

There were numerous groups or dark grey spots surrounded by a white area, which were of firmer consistency than the neighbouring tissue and were situated in the cortical substance of the posterior lobe, the parietal lobe and the central convolutions of the right side. The meninges over these places were thickened and adherent with the brain. Microscopically these centres were found to consist of partly calcified ova, surrounded by vascular connective tissue infiltrated with round cells. Ova were likewise found in the lumen of smaller vessels. At the same time the upper lobes of the left lung contained softened nodules having ova in their centres. The parent worm, however, was not found.

According to Yamagiwa, besides being observed in the lung and brain, cysts and fibrous nodules containing ova have been found in the mediastina, diaphragm, mesentery and omentum; ova also have been seen in the interstitial connective tissue of the liver in hepatic cirrhosis.

Kanamori (*Mitt. a. d. med. Fak. der Kais.-Japan. Univ. zu Tokio*, iv., No. iii., 1898, pp. 129, 145) doubts that the ova (without parent worm) found by Yamagiwa and others in the brain, liver, &c., had anything to do with distomum pulmonale, especially as they exhibited no lid. He is of belief that they belong to another parasite. Kanamori found them in cirrhotic liver and in an *adenoma of the rectum*.

SYMPTOMATOLOGY.

The patients generally have nothing to tell about the commencement of the disease. Very gradually a very slight *cough*, or even only *clearing of the throat*, sets in with a little expectoration, which is most observable in the morning.

The sputum exhibits an exceedingly characteristic appearance. It is thick, viscid and mucus, and shows light and dark red or reddish-brown spots or streaks ; or it may consist of small red or reddish-brown lumps. The colour of the expectoration is caused partly by the admixture of blood and partly by the *ova* described above (page 354). The ova can be discerned with a magnifying-glass as little brownish spots. On being microscopically examined the sputum is found to consist, besides ova, of red and white blood corpuscles, alveolar epithelium, blood pigment in the form of yellow and black flakes, and large and small Charcot-Leyden's crystals ; I once also observed elastic fibres.

The constant occurrence of Charcot-Leyden's crystals is particularly interesting, from the circumstance that they are also frequently observed when other parasites are present. They are found in the sputum of persons suffering from echinococcus in the lungs, and they have been observed in the intestinal evacuations when intestinal worms, particularly anchylostoma, are present (see below).

The number of ova in the sputum varies exceedingly. As a rule, however, it will be found that the more ova there are the more sanguineous is the sputum, and the less blood there is the fewer Charcot-Leyden crystals will be present. Sometimes more than 100 ova will be seen in one preparation, so that several thousands are daily coughed up by the patients. Bälz computes the daily minimum number of eggs expectorated at 12,000.

In rare cases it is observed that the parent distoma also are expectorated. Taylor mentions such a case in Japan.

Occasionally it happens that the blood in the sputum can only be confirmed by the microscope, but on the other hand severe hæmoptysis may set in. Bälz observed a case in which the patient lost nearly a pint of blood within a few hours. This happens particularly after exertion, when coughing and expectoration are apt to provoke the hæmorrhage. The cold season also causes the expectoration to be aggravated.

Exceptionally the patient complains of a feeling of pressure, heat, irritation, or occasional pains in the chest.

The examination of the thorax mostly yields negative results, with the exception of symptoms of bronchitis at isolated spots, enfeebled vesicular respiration, long drawn rough expirations, whistling and fine râles. I repeatedly observed, moreover, that one side, presumably the one that harboured the parasites, breathed less freely than the other.

The nutrition and general condition of the patients generally remain undisturbed.

The cough and sputum often disappear for months and then return.

The disease has a very chronic course. It may persist for ten or even twenty years without causing serious illness.

Taking into consideration the destruction of the lung tissue caused by the worms, this seems remarkable and even incomprehensible. Nevertheless it confirms Leuckart's opinions in a more complete and striking manner than all the observations and experiments hitherto recorded, that in opposition to the prevailing ideas, the lung tissue itself is not markedly sensitive. Even the cough which accompanies the hæmoptysis

only sets in when the cyst containing the worm opens into the bronchi and the contents are discharged into the trachea. The only grave danger which threatens the patient, is that the destruction of the lung tissue may extend to one of the larger vessels and induce severer hæmorrhages. Death from hæmorrhage does not seem to have been observed. Should, however, great hæmorrhages be repeated frequently, the patients become anæmic and easily fatigued ; palpitation, dyspnœa and dropsy ensue, leading to a fatal issue.

The disease is more serious when the distomum takes up its seat in the *brain*, or when its eggs reach this organ through embolism, a condition which the observations of Yamagiwa and Otani, mentioned above, prove. The symptoms of disease set up under these circumstances depend on the part of the brain affected, but principally consist in *epileptiform convulsions* and other symptoms of a *cerebral tumour*.

Otani's patient, a male, aged 26, after having suffered from hæmoptysis for over a year, had *epileptic fits.* They were at first rare, but after four months they suddenly set in very frequently, consciousness was disturbed, and death ensued after two or three weeks under symptoms of collapse.

Yamagiwa's patient, a male, aged 29, exhibited the symptoms of a *cerebral tumour ;* he had epileptiform convulsions which, commencing in the left arm, at first only affected the left half of the body, but later on became universal. He, moreover, suffered from dizziness, right-sided headache, loss of memory, sleeplessness, paresis of the left side of the face and the left arm, a ring of colour in the left eye, indistinct vision in the same eye, all objects appearing prominent to him, though the result of ophthalmoscopic inspection showed the parts to be normal. The convulsions increased in number (104 attacks in one day), and death ensued from gradual exhaustion after a two years' illness. The disturbed vision was due to affection of the posterior part of the brain surface.

In other situations the parasites induce no symptoms. Sometimes ova are found in the stools, owing in all probability to the sputum having been swallowed.

DIAGNOSIS.

The diagnosis of the pulmonary affections induced by distoma is simple enough when on microscopic examination the ova are found in the sputum.

H. de Gouvéa,[1] in 1895, published the case of a French naval officer who, while in America, and after a previous mild fever, had pains in the left lung, severe spasmodic attacks of coughing, accompanied by slight hæmoptysis, and after a three weeks' illness coughed up a living *distomum hepaticum.*

This is the first case in which this parasite, which, on the whole, is very scarce in man, has been observed in the lungs. De Gouvéa, for the diagnosis of similar cases, advises the examination of the sputum for the ova of distomum hepaticum. They are easily distinguishable from the ova of distomum pulmonale by their larger size. The ova of distomum hepaticum, according to Leuckart, are 0·13—0·14 in length and 0·075—0·09mm. in breadth. They resemble other ova in being oval, brown, and in possessing a lid.

Should *cerebral symptoms*, especially epileptiform convulsions or symptoms of a tumour on the brain, be set up in patients suffering from this disease, one must consider the possibility of such symptoms being caused by cysts of worms or emboli of ova in the brain, more especially in countries where distomum pulmonale is endemic. Of course it will be impossible ever to reach a positive diagnosis. The great frequency with

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[1] *La distomatose pulmonaire par la douve du foie.* Paris, 1895.

which, according to my experience, epileptic convulsions occur in Japan, is probably at least partly due to this parasite.

PROGNOSIS.

The prognosis of the disease is, in general, good. Complete recovery, however, has never yet been positively observed, but, provided no very severe pulmonary hæmorrhages set in, there is no direct danger to life. When the affection is complicated with tubercular phthisis the prognosis is unfavourable. The disease is always very grave when the brain is attacked.

PROPHYLAXIS.

In order to prevent the disease, the greatest care must be exercised in the choice of drinking water in those countries where the ailment is endemic. Doubtful water should never be drunk until it has been boiled or filtered. One should avoid eating any raw food-stuffs (fish, snails, mussels, vegetables, &c.), with which the parasite may possibly be conveyed into the body. Yamagiwa's advice also deserves all attention, namely, to collect the sputum of patients in certain vessels and burn it ; patients should never be permitted to spit on the ground or into water. Attention to these details might cause the gradual extinction of the worm.

TREATMENT.

The treatment of this pulmonary disease is symptomatic. Various parasiticidal methods have been tried, partly as internal remedies and partly as inhalations, with negative results.

When the brain is attacked, and when from the symptoms it may be concluded that the disease is superficially situated, an *operation* may be undertaken. This would consist in enucleating the centre of disease after removing the vault of the cranium over it. The results, however, achieved hitherto by this method of treatment have not been very encouraging, for the patients usually succumb from exhaustion, even after the offending seat of disease has been removed.

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(Nos. 1-3, Jena, 1899) contain the most complete register of the literature on parasitic
diseases.

II.

DISTOMUM HEPATICUM.

HISTORY.

IN 1874 McConnell, in Calcutta, discovered a new Distomum in the liver of a China-man who had died from a serious hepatic disease. Soon after the same parasite was discovered in Mauritius by Macgregor, the hosts likewise being Chinamen who had died there. Neither of these observers gave the worm a particular designation, but in the following year—almost simultaneously—it was called *Distomum sinense* by Cobbold and *Distomum spathulatum* by Leuckart. In 1883 Bälz reported the endemic occurrence of two hepatic distoma in Japan; these he considered new, and designated them *Distomum hepatis endemicum s. perniciosum* and *Distomum hepatis innocuum*, respectively. Leuckart, however, pointed out that in Bälz's discovery it was not the question of two different forms but of one and the same parasite, which was identical with the one discovered by McConnell.

Ijima, in Japan, found the same worm in the cat.
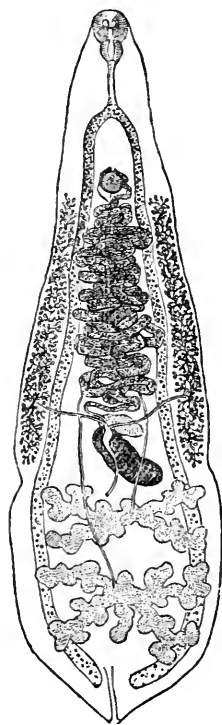
FIG. 33. — *Distomum spathulatum* (enlarged 15 times). After Leuckart.

NATURAL HISTORY.

Leuckart described *Distomum spathulatum* (see fig. 33) as a slender, flat worm, about 10 to 13 mm. in length and 2 to 3 mm. in breadth. In its living state it is almost transparent. The anterior part of the body is narrowed to a lancet shape, tapering from the ventral sucker forwards; the posterior end is inclined to be somewhat pointed. The skin is smooth. The oral sucker is larger than the ventral, which is situated at about a quarter of the entire length of the worm from the oral sucker. The œsophagus is short; the intestinal diverticula, on the other hand, are of considerable length and reach to the end of the body. In the posterior quarter of the body two conspicuous testicles are seen, one behind the other, and more towards the front the vesiculæ seminales, ovaries and uterus are placed consecutively, the latter extending as far as the ventral sucker. Close in front of the latter the uterus, together with the seminal tubules, originating from the two vasa deferentia, open into a small sexual cloaca. The long vitelline sacs are situated superficially to the intestinal ramification, and extend along the margin of the body on either side, their excretory ducts running across to the ovary.

The eggs, which are 0·028 to 0·03 mm. in length and 0·016 to 0·017 mm. in breadth, are of a brownish or black colour, with a thin shell. When mature

they exhibit a little lid, set within with a groove at the narrow end, while at the blunt end appears a tiny knob. (Bälz).

The development of the embryo proceeds within the worm, and cilia appear whilst the embryo is within the parent.

PATHOLOGICAL ANATOMY.

The parasites in great numbers, it may be even in hundreds, are found in cyst-like recesses or sinuses of the *walls of the largely dilated gall bladder and bile ducts.* In size these cysts vary from a hazel-nut to that of a walnut.

The cysts are undoubtedly connected with the bile ducts, so that isolated worms are occasionally found free in them and in the duodenum. In the gall bladder and ducts the worms cling to the mucous membranes by means of their suckers. Ova are found in great numbers not only in the recesses of the gall bladder and the bile ducts, but also in the upper part of the intestinal canal.

The liver is much enlarged, and is either of normal colour or of a darker tinge in consequence of hyperæmia. The tissues around the cysts and bile ducts are atrophic. Enlargement of the spleen, intestinal catarrh, ascites and œdema are concomitant conditions usually present in this affection.

Miura found numerous submiliary, miliary and somewhat larger prominences on the peritoneum of a Japanese who had died of beri-beri. On microscopical examination these nodules were found to be fibrous nodules, in the centre of each of which one or more ova of worms were found, with some giant cells. The nodules seemed to be connected with the lymphatics. Miura considers that the ova were those of Distomum spathulatum. During life no symptoms of this affection had been exhibited.

GEOGRAPHICAL DISTRIBUTION AND ETIOLOGY.

China, Tonquin, and *Japan* are the only countries in which the Distomum hepaticum has been met with.

In Japan, according to Taylor, there are several narrowly circumscribed centres in which it appears endemically, namely, one in the vicinity of Okayama in the Bizen Ken, a second near Sendai, in the Miyege Ken, and a third in the Shinano province. There are, moreover, one or two centres also in the provinces Higo and Hizen on the island of Kiushiu. Probably the ailment is more widely distributed in Japan ; for in Kioto I observed numerous liver ailments the nature of which could not be confirmed, and which probably may have been caused by this parasite.

The principal centre in the Okayama province is situated on a strip of the coast which was recently reclaimed from the sea, and is principally used for the cultivation of rice. Bälz states that 20 per cent. of the inhabitants, or even more, are affected by the parasite. A dam protects this strip of land from the rising tide, and there is a canal with almost stagnant water along its entire length. All the infected villages are situated along this canal, which presumably must have some connection with the prevalence of the parasite there. Ijima states that the water from this canal is not used for drinking purposes, but for cleaning kitchen utensils and washing vegetables which are mostly consumed in a half-cooked condition. Moreover, the passing boats, with barrels containing excrement used for manuring the fields, pass along these waters. Under such circumstances, Leuckart conjectures that the Distomum spathulatum

spends the first part of its life in some mollusc (perhaps a snail) inhabiting the canal water, and then either migrates into man's body direct with its host, or leaves the latter while still immature, and only later after encapsulation succeeds, with the help of a second intermediary host, in invading man, or accomplishes this object through clinging to some article of vegetable diet. Japanese, like Chinese, are in the habit of eating many foods, animal as well as vegetable, raw or only half cooked, a custom that favours transmissions of this kind.

The disease attacks all sexes, ages and constitutions, without distinction; even little children are not spared. It is not rare in one family to find parents and children simultaneously suffering from the disease.

SYMPTOMATOLOGY.

The signs and symptoms present in persons suffering from distomum spathulatum are, according to Bälz and Taylor, as follows :—

A morbid appetite develops, and a considerable *enlargement of the liver* gradually sets in, accompanied by a sensation of pressure and weight in the epigastrium, which slowly increases in intensity. The hepatic enlargement can be confirmed by palpation and percussion, and even by inspection. The enlarged organ often extends to the umbilicus, and has a hard smooth margin as in amyloid liver. It is only exceptionally that the border or anterior surface is felt to be uneven. Occasionally the enlargement is confined to the left lobe of the liver, and in rare cases may even be entirely absent. The liver is usually more or less painful on pressure. There is often jaundice, which is sometimes intermittent. The spleen is, as a rule, distinctly enlarged.

The general health and nutrition often remain fairly good for several years. Bälz saw persons working in the fields although they had had the disease for six years. Sooner or later, however, in spite of eating plenty, nutrition deteriorates and *diarrhœa* sets in. Diarrhœa occasionally occurs even from the commencement of the disease, but is at first irregular and intermittent. Gradually the attacks become more frequent and last longer, until there is barely an interval between them. The stools average about twelve daily ; they occasionally, or may even constantly in some cases, contain blood. As a rule there is no fever, but the pulse often increases to 85—100 beats per minute. During the further course of the disease ascites and dropsy in the legs appear, at first only intermittently, and the patients becoming more and more enfeebled and cachectic finally succumb to general exhaustion.

Leuckart draws attention to the fact that the symptoms of disease exhibited by patients afflicted with distomum spathulatum bear an unmistakable similarity to those of *dry rot* in horned cattle, due to the distomum hepaticum, though the course of the former disease is slower.

In many cases the subjective and objective symptoms of the disease are very trifling, or may even be entirely absent, so that the parasites are only incidentally found in small numbers in the dilated bile ducts. It was this circumstance which led Bälz to differentiate a particular distomum innocuum.

In the cases observed by Macgregor there were, beside the symptoms indicating the hepatic disease, *paralytic affections*, particularly of the limbs, such as sometimes are seen after lead poisoning. Macgregor was inclined to attribute these symptoms likewise to the parasites, and held them to be of a reflex character, or to be induced by a toxin originated by

the parasites ; but as symptoms of this kind were never observed in any of McConnell's cases, or in any of the numerous cases observed in Japan, Macgregor's observations were no doubt due to an incidental complication (beri-beri ?).

DIAGNOSIS.

The diagnosis of the disease is founded on the *microscopical proof* of the characteristic *eggs* of the distomum in the intestinal evacuations of the patients.

PROGNOSIS.

The prognosis is *unfavourable*.   Hitherto no recovery from the disease has ever been observed.

TREATMENT.

The treatment is *symptomatic*.   The administration of anthelmintics are, in all cases, justifiable.

The *distomum conjunctum* observed by McConnell in Calcutta, in great numbers in the thickened and dilated bile ducts of two Mohammedans who died of dysentery, are related to, but not identical with, distomum spathulatum (one difference amongst others consisting in a cuticle beset with little spikes or hairs) ; the liver in one of McConnell's cases was enlarged and somewhat degenerated (fatty).   The distoma had already been previously found by Lewis and Cunningham in the liver of Indian pariah dogs, and still earlier was discovered by Cobbold in the liver of the American fox.   Leuckart, however, calls the identity of the Indian and American distomum in question.[1]

Winogradoff, in Siberia (Tomsk), frequently found in man a species of distomum which he designated *distomum sibiricum*.   They were found in great numbers, 200 and upwards, in the dilated bile ducts and incidentally in the intestine also.   In addition there was hepatic cirrhosis, with dilatation of the bile ducts and brown atrophy of the hepatic tissue and ascites.   If the distoma leave the liver and enter the intestine, Winogradoff asserts that the cirrhosis may again disappear.   In none of the cases observed by this author had death been caused directly by the hepatic disease, but was the result of other intercurrent diseases, such as pulmonary tuberculosis, inflammation of the lungs, heart disease, &c.   The same distomum was also found by Winogradoff in the liver of cats and dogs.   According to Braun, it is identical with the *distomum felineum*, Rivolta,[2] found in cats and dogs in Europe, in Italy, Germany, &c., as well as in North America.

Jogendro Nath Ghose and E. Mackenzie, at the Indian Medical Congress of 1894,[3] reported the occurrence of a form of *biliary cirrhosis of the liver* in little Hindoo children up to about 4 years of age, in various districts of India (North Bengal, the Presidency of Bombay).   The disease was independent of malaria, syphilis, scrofula, &c., and, as a rule, began at the age of 7 or 8 months, during dentition, with slight fever and gastric disorders, and with considerable painless enlargement of the liver (which, according to Ghose, subsequently shrunk quickly, while Mackenzie at the autopsy always found it enlarged).   There was icterus, ascites, splenic enlargement, œdema, and sometimes even vomiting of blood at the commencement ; in most cases death was occasioned by cholæmia from a few months up to a year ; in rapid cases in two or three weeks.   The cause of the disease is unknown ; the two observers are inclined to attribute it to unsuitable nourishment, such as the eating of spices by the infants, or by the mother while suckling them.

It seems to me more probable that the disease is of a *parasitic character*, and in accordance with what we know, the distomum most likely has something to do with it.

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[1] Leuckart, *Die Parasiten des Menschen*, 2nd edition, 1889, 1—4, p. 355.

[2] Braun, *Ueber ein für den Menschen neues Distomum aus der Leber. Cbl. f Bakteriol. u. Parasitenk*, 1894, No. 16, p. 602.

[3] *The Lancet*, 1895, Feb. 2, p. 321.

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III.

BILHARZIA DISEASE.

SYNONYMS.

Bilharziose, Hématurie bilharzienne.

HISTORY.

Distomum hæmatobium was discovered in Cairo by Bilharz in 1851, and recognised to be of clinical importance. Cobbold called it *Bilharzia hæmatobia*, out of compliment to its discoverer, and this designation has been universally accepted. The morbid disturbances originated by this parasite were known long ago, but were confused with other diseases. As long ago as 1591 Prosper Albinus, in his " Medicina Ægyptiorum," mentioned the frequency of urinary calculi in Egypt, and Renault reported the frequent occurrence of hæmaturia amongst the French troops at the time of the occupation of Egypt by Napoleon (1798-1799). Harley, in 1864, found the Bilharzia in Cape Colony (Distomum capense), and later on there were reports of its occurrence in many other districts of Africa.

GEOGRAPHICAL DISTRIBUTION.

The geographical region of distribution of Bilharzial disease extends over a *large part of Africa*. *Egypt*, particularly the basin of the lower Nile, forms the principal centre; from one-third to one-half of the native population (Fellahs and Copts) being said to be affected. Bilharz and Griesinger, in Cairo, found this parasite in 117 times out of 363 autopsies. Sonsino, in Cairo, and in other places of Lower Egypt, came across this parasite 42 times in 91 autopsies. Besides being in Egypt, the parasite is also endemic in the whole of East Africa and as far south as the Cape of Good Hope; moreover, in Angola, in the Congo State (F. Plehn only saw imported cases in Cameroon), on the Gold Coast, in Tunis, and in Algiers, the presence of the parasite has been reported. It probably also exists in many other parts of Africa where there is endemic hæmaturia, as in the Soudan, in the countries adjacent to the south-eastern Sahara, on the White Nile, in the neighbourhood of the lakes Albert and Nyassa, and in the basin of the Zambesi.

The incidence of this disease is, however, not confined to Africa. It has lately been found in Mauritius and in Syria (Wortabeh), in Mecca (Hatch, in Bombay, at all events often found the disease in Mohammedans, who, according to their account, had been infected in Mecca), in Mesopotamia (Sturrock), in Penang (Schön), and in Shanghai (Jedelius). Quite recently Walker[1] even saw a case in North America (Sparta, Illinois).[2]

[1] *Medical Record*, 1900, February 24.
[2] In the province of Canton in China, urinary calculi are remarkably frequent. When I visited the hospital of the Medical Missionary Society in Canton, Dr. Kerr, who had

The *Bilharzia hæmatobia* (see fig. 34) is a *trematode* with distinct sexes, and macroscopically very similar to a small round worm. It possesses two sucking discs on the front of the body, an oral and a ventral sucker ; the intestinal canal commences at the former and terminates at the latter. The worm being hæmatophagous, the intestine frequently contains blood. The *male*, according to Leuckart, is 12 to 15 mm. in length, and 0·5 mm. in breadth at the thickest part, and is of a dirty white colour. The anterior part of the body is tapered off and flattened, while the thick posterior part of the body has a cylindrical appearance with its edges curving inwards towards the abdomen, whereby a groove or not quite closed tube—the canalis gynæcophorus—is formed, which serves for the reception of the thin female worm. At the termination of this canal the sexual opening (without penis) is situated, the semen is discharged into the canal and is probably taken up by the sheath of the female through imbibition (Sonsino). The dorsal surface is provided with small spinous papillæ by means of which the males cling to the walls of the veins during their wanderings. The *female*, according to Leuckart, is 16 to 20 mm. in length, and about 0·2 mm. in breadth, it is filamentous, and at the posterior part of a dark brownish, or even blackish, colour, this being caused by the contents of the intestine (see above). It lies in the canalis gynæcophorus of the male, with its head directed to the front, and as it usually is longer than the male its ends, more particularly the posterior end, protrude free beyond. Its sexual orifice is close behind the ventral sucker. The number of females found is always less than that of the males (Kartulis).
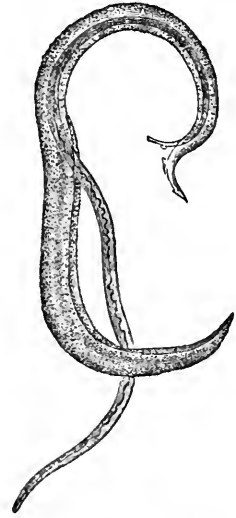
Fig. 34. — *Bilharzia hæmatobia*, male and female, the latter in the canalis gynæcophorus of the former; 10 times enlarged. After Leuckart.

The eggs (see fig. 35) are oval, of a yellowish colour, slightly transparent, and provided with a thin shell without lid, and a small spine, which is mostly at the hinder end, more rarely on one side, and is sometimes absent. The size of the eggs varies. According to Leuckart, they

officiated for many years as surgeon there, informed me that he had had about 600 operations for stone ; in 1881 alone he had operated on 60 cases. In most cases the calculi consisted of uric acid. In Canton a large part of the population live on the Pearl River, some on anchored boats, some on houses erected on piles, or rafts. The river water is used for cooking and drinking, while excrement is deposited direct into the river. Two-thirds of Kerr's stone patients were persons whose occupation brought them into close connection with the river, boatmen representing the largest contingent (see Carrow's Report in China, Imp. Mar. Cust. Med. Rep., eighteenth issue, 1880, and Report of the Medical Missionary Society in China for 1881). It therefore seems rational to connect stone disease with the river. But in this connection I think less of the chalky constituents of the water, which are often blamed as the cause of urinary calculi, than of a *parasite* that lives in the water, and I consider it would be advisable to direct attention as to the occurrence of *distomum hæmatobium* in Canton.

In Bangkok (Siam) the river Menam plays a similar part to that of the Pearl River in Canton, and here likewise urinary calculi are frequent. Of this I was personally informed during my visit to the hospital by the native doctor who conducted it, and his information was subsequently confirmed by letter by Dr. Rasch. In the Laosland, according to the verbal information of the traveller, Carl Bock, stone complaints are also very frequent, particularly in Lampoon, a town situated on a tributary of the River Meping, near Cheng-mai.

measure 0·12 mm. to 0·04 mm. (without the terminal spine, which measures 0·02 mm.) ; according to Sonsino they measure 0·16 mm. to 0·06 mm. ; according to Looss, who described the eggs as of a short spindle-shape, bigger in the centre and carrying a small opaque point at the posterior end ; the total length averages 0·197 mm., the greatest breadth 0·073 mm., and the spine barely more than 0·0081 mm.

The eggs passed by the patients in the urine often contain a fully-developed embryo ready to emerge. Others are not transparent, and their contents having perished become calcified. According to Lortet and Vialleton the latter occur only in decomposed, not in normal urine.

The *freed embryo* has remarkably lively movements, during which it continually changes its shape. Its normal form, according to Looss, is an extended cylinder with its lateral edges slightly bent inwards. It possesses on its somewhat more massive anterior end a papillary process, and is provided up to this point with a thick ciliated covering. Besides this, one may observe on the outer aspect of the body two transverse rows of very delicate cones ; they lie close behind the head and somewhat behind the centre of the body, and are arranged circularly round the body (Looss). The process on the head has a central orifice which communicates with a cyst-like organ, an embryonal stomach sac, containing numerous tiny, light-refracting granules. On either side of the sac a pear-shaped formation is observed, which is considered by Railliet and Looss to be a single-celled gland. The posterior part of the body is crammed with numerous pale cells, which, according to Looss, are only germ cells. A highly-developed vascular system and two pairs of ciliated funnels into which the former discharge, may, moreover, be distinguished in the embryo.

FIG. 35.—Eggs of *Bilharzia hæmatobia*. *a*, with terminal process ; *b*, with lateral process. After Bilharz.

If the eggs are placed in pure water it is possible to follow, under the microscope, how very soon the shells burst and the embryos slip out and move rapidly hither and thither. They remain alive in water for a long time, but die in urine after twenty-four hours. *The further development of the embryo is still unknown.*

According to the analogy of other distoma is must be assumed that the embryo enters some animal which inhabits water, where it is transformed into an embryonic chrysalis (redia, sporocysts), which begets in its interior a generation of immature distoma ; that these again become free, perhaps seek a second intermediary host, become encysted, and thus become larvæ, which finally, with their bearer, are taken up by their definitive host—man—and then develop into their adult form. But all experiments conducted by various observers with mollusca, crustacea, larvæ of insects, small worms, fishes, and plants have yielded negative results. Sonsino, for a time, was of opinion that he had discovered the intermediary hosts of Bilharzia in various kinds of water arthropods, but he afterwards himself contradicted the correctness of his own discovery. Looss therefore believes that the embryo invades man direct, becomes a sporocyst, which then deposits its brood in its bearer, a conjecture which Leuckart had already previously announced. Grassi, on the grounds of experiments conducted on sheep with Bilharzia crassa, asserts that the embryo is transformed into the adult worm without a change of generation; but according to Looss the existence of a typical discus proligerus in the posterior part of the embryo contradicts the possibility of this. Experiments conducted by Looss on monkeys of different species (in which Cobbold had also found a Bilharzia) by giving them water containing embryos to drink, had negative results, but he found that the embryos perished when exposed to the effect of the mucous membrane of a monkey that had been killed. He is therefore of opinion that the embryos penetrate, not through the stomach, but through *the skin;* but he furnishes no proof of his opinion. He, however, supports his views from the fact of the presence of the two glands in the front part of the body of the embryos, which he

identifies with the spinous glands of some immature distoma, the secretion of which exercises a softening influence on the skin of the larvæ of frogs and insects; and also in the facts brought forward by Brock, which will be mentioned below.

The life of the *worm* is probably a long one. Sonsino mentions the case of an Egyptian who left his native country as a boy when he was suffering from hæmaturia; he lived in France for nine years, and on returning home he certainly was no longer suffering from hæmaturia, but in the last drops of urine living eggs were still evacuated.

ETIOLOGY.

The *Bilharzia parasite* principally affects *natives*, whereas Europeans are only exceptionally attacked. In Cape Colony also, the disease is often observed in coolies imported from Bombay and Madras.

The *male sex* is attacked far more frequently than the female sex. *Country* people are particularly prone to the complaint.

As we do not know the history of the development of the Bilharzia, we know nothing definite as to the manner by which infection occurs. It is conjectured that the parasite is *taken into the stomach* either with impure drinking water or raw food, in some mollusc, fish or vegetable (Griesinger and Bilharz), or that it invades the body *while bathing*, or through the *skin, the urethra, or the anus* (Harley, Allen, Guillemard, Brock, Looss).

The *drinking water theory* is strengthened by the fact that the disease occurs most frequently amongst the country people, who, during their work, often drink the water from rivers and canals into which bathers have previously evacuated their fæces, or from ditches and pools in the fields which have also been polluted by excrement; Europeans who only drink filtered water are therefore not so liable to the disease. It may also be noted that the disease is rare in Cairo and Alexandria where the Nile water, though not well filtered, is subjected to purification, in comparison with the small towns and villages where the water is not purified (Sonsino).

The etiological importance of *bathing* is strengthened by the observation made in South Africa that the members of the male sex, who are more liable to Bilharzia than the female sex, are in the habit of bathing frequently in rivers and lakes and swim about in the water during a great part of the day, while on the other hand the women and girls, who are very rarely attacked, seldom bathe and swim, while both sexes drink the same water. Brock reports from the Transvaal that for the reason given boys are so very often affected that the natives are apt to ascribe the loss of blood during urination to a physiological cause analogous to that of menstruation. Allen regards the long prepuce of the boys as particularly apt to take up the parasites through the urethra. In Natal the Kaffirs during bathing have the habit of tying a string round the penis to guard against infection. In Egypt the fellahs, who during high water are obliged to remain knee deep in the water for hours at a stretch while cultivating the fields, are more liable to the disease than those Egyptians who are not agriculturists. According to these observations, the bathing theory appears to be the more plausible. Nevertheless the fact must not be disregarded that bathing always affords the opportunity of swallowing water.

Harley observed that the colonists in Cape Colony often suffer from nodular excrescences of the skin, which later on become transformed into indolent ulcers, which when healed leave large cicatrices. He is of opinion that these boils are consequent upon the invasion of the parasites into the skin during bathing.

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According to Griesinger's observations in Egypt, the months June to August yield the most numerous cases of Bilharzia disease (the Nile rises from July to September), while from October to January there are but few cases. Sonsino, however, could not confirm this observation, as he found that season had no influence on the number of cases of illness.

The *period of incubation* in Bilharzial disease appears to be short. One of Hatch's patients in Bombay, who stayed in Suez for a fortnight, was taken ill only four weeks after his return. Brock, on the other hand, on the ground of his experience, states that incubation takes four months.

PATHOLOGICAL ANATOMY.

The trunk of the *portal vein* with its tributary intestinal branches, and more especially the *venous plexuses of the urinary apparatus and rectum*, are the particular *seat* of Bilharzia hæmatobia. The worms are occasionally found free in the urinary passages.

Kartulis, in thirty-three cases he examined, found distoma six times in the *vena cava inferior*, and once in the *right common iliac vein*. He came across neither female worms nor eggs in the veins of the *spleen, pancreas*, or *stomach*. According to Lortet and Vialleton, the females deposit their eggs in the parts of the body whence they can easily be expelled.

In order to find the worms in the portal vein, it is advisable, before opening it, to tie it at either end (Sonsino), and then to spread the blood on a glass plate and examine it with transmitted light (Schiess-Bey).

In regard to the connection between the veins of the bladder and the portal vein, it may be remarked that the former are connected with the rectal veins through the prostatic plexus into which some part of them discharge; and that the rectal veins partly discharge direct into the portal vein through the superior hæmorrhoidal veins, and partly flow into the inferior vena cava by way of the middle and inferior hæmorrhoidal veins, and the plexus Santorini connected therewith, the inferior vena cava being really likewise connected with the portal vein (Sachs-Bey). The veins of the ureter and kidneys are also directly connected with the inferior mesenteric vein.

At the period of puberty the worms in pairs, assisted by the locomotion of the male, descend into the veins of the urinary bladder and rectum, there to deposit their eggs in large numbers, this being the reason that the parasites are found most abundantly in the veins of the pelvic organs. The number of worms found in a single person is occasionally very large; in one case Kartulis found 300. The eggs deposited in the vessels cause engorgement of the small veins and capillaries, which are finally torn or bored through by the spinous process of the eggs, so that the latter are released into the surrounding tissue, where they agglomerate and form the point of departure of inflammatory changes. Bilharz has suitably designated this condition *infarcimento bilharzico*, or *Bilharzial infarction*. The degree of inflammation set up varies, and depends not only on the number of eggs and the duration of the disease, but on which organ or tissue is affected.

The *urinary bladder* in the dead body is found to be affected most frequently and most severely. In the milder cases the symptoms exhibited are those of a more or less intense catarrhal inflammation. The mucous membrane in places is reddened, swollen and covered with a blood-stained mucus containing numerous eggs, and here and there exhibits nodules caused by agglomerations of eggs, which, according to Sonsino, commence as transparent or opaline blisters or papules not exceeding the size of a millet seed. In far advanced cases, larger nodules or slightly raised lamella are found, particularly on the posterior wall of

the bladder ; the lamella are of a round form and of a yellow, brown or grey colour, and of a leather-like consistence, or so hard that they crunch on being cut into. Their surface is rough and covered with sand-like coating, consisting of eggs, egg-shells, and deposits of urates intermixed ; sometimes also the surface is ulcerated. There are, besides, excrescences of soft consistency and great vascularity, which appear villous or polypoid, or resemble cock's-combs ; they exhibit a coating similar to the lamella, and their surface is likewise occasionally eroded or ulcerated. The wall of the bladder, moreover, is more or less thickened, hypertrophy of the muscles contributing to this appearance ; the cavity is lessened in size and sometimes quite filled with excrescences. In other cases, on the contrary, the bladder is dilated.

Often *urinary calculi* are found in the bladder, as well as in the ureters, or in the pelvis of the kidney. According to the observations made in Egypt the stones mostly consist of oxalate of lime, which may have some connection with the oxalic acid contained in vegetables, which are the staple food of the population. Various observers have found eggs in the nucleus of the stones, while other investigators were unable to prove their presence. The great frequency of urinary calculi in Egypt has already been mentioned ; according to Colloridi 80 per cent. of the cases are to be traced to Bilharzial disease.

Microscopical investigation shows that the lamella and excrescences described above are mostly formed of the hypertrophied sub-mucosa, which, like the mucosa, is infiltrated with leucocytes which occasionally lie so close together that unmistakable abscesses are formed ; enormous numbers of eggs, also, are deposited, which are partly calcified and thus cause the hard consistency of the lamella. The mucosa, also, contains numerous eggs, which, however, are not quite so plentiful as in the sub-mucosa. Rütimeyer also found eggs at isolated places close under the intact covering of epithelium, together with pus corpuscles in roundish, undoubtedly pre-formed spaces, which correspond with the little blebs or papules described by Sonsino ; undoubtedly it is from such spots that the eggs become free and gain the interior of the bladder when the epithelial cover tears. On rare occasions eggs have also been found in the musc es, close below the peritoneal covering of the bladder. Griesinger in one case observed excrescences of cock's-comb shape on the peritoneal covering.

The mucous membrane of the *ureters* and even the pelvis of the kidney often exhibits the same changes as the bladder. These changes cause strictures with dilatation behind them, and when the lumen is completely blocked by a stone may lead to hydronephrosis with atrophy of the renal parenchyma. More frequently, however, cystic pyelitis and parenchymatous and interstitial nephritis are observed as sequelæ, and also formation of cysts and renal abscesses. Different observers have also perceived eggs in the tissues of the kidneys.

Next to the bladder, according to Sonsino, the *seminal vesicles* are most frequently and severely affected. The walls are found to be thickened, infiltrated and permeated by more or less calcified eggs, and as the latter are also found on the surface of the mucous membrane, it is possible that they may be transferred to the semen.

In the *prostate* chronic inflammation is set up by the deposit of eggs ; this part is therefore always enlarged, attaining the size of an apple, and becoming quite hard.

In rare cases the *female genital organs* also become diseased primarily as well as secondarily and exhibit similar changes to those of the bladder described above. Madden published a case from Egypt in which the

disease was even confined to the vagina.   Occasionally vesico-vaginal fistulæ are observed as a consequence of the disease of the bladder.

Similar changes also occur in the *rectum*.   As in the bladder, the eggs are most numerous in the submucosa, less numerous in the mucosa, and are very rarely found in the hypertrophied muscles.   The polypoid excrescences originate principally from the severely hypertrophied glandular layers (Zancarol, Damaschino, Rütimeyer).   Small, flat ulcerations, only affecting the mucous membrane, are met with.

With Bilharzial disease as a basis *carcinoma* or other new formations often develop.   Kartulis compiled 300 cases, and found carcinoma ten times (nine times primary), once sarcoma of the bladder, three times carcinoma of the prostate (once primary), once fibro-adenoma of the prostate, twice carcinoma of the seminal vesicles (secondary), and once carcinoma of the rectum (primary).

Kartulis, in a fellah, 30 years of age, observed an *epithelioma of the right foot and leg* in which eggs were found partly in the hypertrophic papillæ of the skin, partly in the corium.   The majority of the eggs were calcified or only shells or *débris* of eggs were present.   The capillaries were free from eggs.   The urine contained neither albumen nor sugar, but was not examined microscopically.   Kartulis is of opinion that in this case the transmission of the parasites had taken place *directly through the skin*.

Besides the organs already mentioned, the presence of eggs has been seen in extravasation of blood, and in the enlarged *mesenteric glands ;* they have likewise been found in the *lungs* with small interstitial infiltrations, in the *liver* with slight cirrhotic changes, and in the *cutis*. Gautrelet found the eggs in a *gall stone*, which a woman passed who had previously lived in Egypt twenty years.   Greisinger in one case observed three egg shells in the *blood of the left ventricle*.   The eggs hitherto have not been found in the spleen or pancreas (Kartulis).

Angelica G. Panagiotatos[1] in one case observed *pleurisy with chylous effusion*, and at the autopsy found the pleura thickened, opaque, and with dilated vessels and polypoid proliferations which, in microscopical sections, showed eggs in various stages of development.

The transmission of the eggs from the usual seat of the parasites to distant parts of the body takes place partly through the venous blood (to the lungs through the anastomoses between the venous net work of the urinary blood with the vena hypogastrica and vena cava inferior), and partly with the assistance of their spinous process and the influence of external pressure (into the left ventricle from the lung).

Kartulis is of opinion that the eggs are not transported to distant parts of the body through the current of the blood, but are directly deposited in the organs in which they are found.

SYMPTOMATOLOGY.

Hæmaturia is the principal symptom of Bilharzial disease ; it appears first intermittently, and later becomes permanent.   In mild cases only the last drops at each micturition is tinged with blood or consists of pure blood only, and is induced by the almost empty bladder contracting strongly, thus causing the vessels filled with eggs to burst.   The patients are obliged to urinate frequently ; there is no actual pain, but only a slight pricking at the prepuce or root of the penis, more particularly when passing urine.

[1] *Janus*, 1900-1, v., p. 51.

If the urine is allowed to stand, the flocculent blood-tinged mucus settles at the bottom of the vessel, while in other respects the urine is quite normal. On microscopically examining the sediment there will be found besides red and white blood corpuscles and epithelium, the eggs described above and empty egg shells; with these there is at times crystals of uric acid, urate of ammonia, oxalate of lime and triple phosphates. Sometimes the patients evacuate the eggs in hundreds and thousands.

A transient increase of hæmaturia is sometimes observed after bodily exertion, shaking of the body (as by railway travelling) and excesses in eating and drinking.

In further advanced cases, the patients complain of pressure and severe burning pains which may radiate to the perinæum, the anus, the abdomen and the lumbar region; the abdomen and lumbar regions may also be painful on pressure. The urine assumes a more uniform sanguineous colouring, loses its normal consistency, becomes alkaline and opaque, and deposits a more or less plentiful sediment of blood. Owing to the formation of coagula the urethra may be obstructed, and transient dysuria and ischuria may occur in consequence. Occasionally, also, paroxysms of pain obtain, which are very similar to renal colic, and are caused by the passage of blood clots through the ureters.

In severe cases the hæmaturia and cystitis increase, and in consequence of the latter condition *gravel* and *urinary calculi* form. The pains become more severe, the urine is still further mixed with pus, and spasm of the bladder, dysuria and ischuria, set in. Renal colic is also observed. Perhaps even more frequently than stone in the bladder *urinary fistulæ* occur. According to Trekaki and v. Eichstorff, these are present in 40 per cent. of the cases, and arise from peri-urethral inflammation and subsequent abscesses in the tissue through agglomerations of ova. The most ordinary fistulæ are perineal, scrotal or penile; fistulæ are found more rarely in the gluteal region, on the upper part of the inner aspect of the thigh and at the nates. The latter, according to Kartulis, may be due to the invasion by ova of the hypogastric and sacral veins, but may on the other hand be caused by direct infection from the skin. The external orifice of the fistula has sometimes a wart-like excrescence that may attain the size of a filbert. Strictures of the urethra are of rare occurrence.

When the *seminal vesicles* are affected, abnormal escape of semen or spermatorrhœa, according to Sonsino, occur, and the semen may be mixed with blood and contain eggs.

Disease of the *prostate* increases the disorders of the bladder and causes violent strangury and painful urination. Enlargement of the prostate is frequently to be made out by rectal examination.

When the disease has its seat in the *female genitals*, a sanguineous discharge containing ova is often observed.

When the *rectum* is affected a further group of symptoms is added to the category of the disease. At first they simulate hæmorrhoidal disorders, and consist of loss of blood, particularly towards the end of defæcation, itching, slight pain at the lower end of the rectum, and slight tenesmus; later on a dysenteric condition sets in. The wall of the rectum on digital examination is found studded with small, soft excrescences. Mackie observed cases in which the disease was confined to the rectum, without participation of the uro-poetic system.

The presence of the ova of Bilharzia in the *liver* and *lungs* does not cause any apparent disorder.

The disease runs a very *chronic course*. In mild cases it may drag on

for years, without causing any deterioration of the general condition of the patients, who may live to a great age. When the parasites die off or are evacuated, and no new infections ensue, the hæmaturia may gradually diminish and the disease disappear. Disappearance of the hæmaturia, however, is by no means synonymous with recovery, for frequently, notwithstanding the entire cessation of the hæmaturia, fresh eggs may still be demonstrated in the last drops of the urine, and in the further course of such cases gravel and urinary calculi may form (Sonsino). In serious cases, in consequence of the continuous loss of blood, disorders of the rectum, anæmia, weakness and emaciation may gradually ensue, and the patient may finally die of general exhaustion; or death may ensue in consequence of uræmic or pyæmic conditions, or in chronic disease of the bladder.

Exceptionally, Bilharzial disease may run an acute course, causing death in a short time. Griesinger mentions two cases which terminated fatally after the short duration of an obscure disease, in which the autopsy revealed nothing beyond fresh Bilharzial disease, with catarrh of the bladder and renal tracts and diffuse hyperæmia of the kidneys.

DIAGNOSIS.

The diagnosis of Bilharzial disease is founded upon *microscopical proof of the presence of the eggs* in the urine, the stools, the semen, &c. The eggs are so characteristic that it is hardly possible to confuse them with those of any other of the parasites of man.

When the *rectum* is diseased the diagnosis may be assured by the excision and microscopical examination of the rectal excrescences. The presence of vesical calculi is confirmed by examination with sounds; care must, however, be exercised not to mistake the hard, rounded lamellæ with their sandy coatings occurring on the mucous membrane of the bladder for calculi.

PROGNOSIS.

Though Bilharzial disease often only originates trifling disorders, which may heal spontaneously, it must nevertheless be regarded as a serious ailment, as in many cases death is due, not so much to the disease itself, but to the disturbances it brings in its train. Patients suffering from this disease are therefore not accepted by the life insurance companies (Brock). The disease does not occur with equal severity in different countries: in Cape Colony it is less serious than in Egypt, because in the latter country the possibility of a fresh infection is more likely than in the Cape.

PROPHYLAXIS.

So long as the history of the development of Bilharzia is unknown, and we are not aware for certain in what way the worm invades the human body, so long must there also be uncertainty as to the prophylactic measures to be adopted. If the statement is accepted that the invasion of the brood of immature distoma, or their intermediary host, takes place through drinking impure water, or eating raw foods, or through bathing, it is urgently necessary to exercise the greatest care in the choice of drinking-water—only to drink doubtful water after filtering or boiling it;

to eschew the eating of all raw foods (mollusca, fish, vegetables, &c.), and not to bathe in rivers or lakes that may be possibly infected.

Allen, for the reasons stated above (p. 369), advises *circumcision* prophylactically, and even conjectures that the ancient Egyptians and Jews originally adopted this custom to protect themselves from Bilharzial disease.

In any case, however, Looss's suggestion should be adopted, that to prevent the further spread of the disease, efforts should be made to render the *eggs of the worms that are ejected harmless* ; with this view, persons suffering from hæmaturia, &c., should never allow their evacuation to go into the water, but should always use separate or dry closets where the embryos are unable to escape and develop further.

TREATMENT.

The treatment of Bilharzia disease is mostly *symptomatic*. Hitherto we have become acquainted with no method by means of which we are able to expel or kill the parasites. This is not astonishing considering their sheltered position, quite apart from the fact that the disorders originated by the parasites would not be terminated by their death and expulsion. The local application of strong *anthelmintics* in the form of injections into the bladder is to be strenuously avoided,[1] as they are not only useless—it being impossible thus to affect a parasite the principal seat of which is in the portal vein—but are also capable of causing severe cystitis. The same objections do not apply to the internal administration of parasiticidal drugs. Wortabeh and Barth recommend oleum terebinthinæ (one teaspoonful three times a day with a little milk) ; Ruault advises extractum filicis liquidum (1—3 capsules per diem up to 0·6 before meals to be continued several weeks) ; Harley prescribes a combination of both drugs (ol. terebinth. 10·0, extr. filicis, chloroform, āā gtts. v., mucil. tragacanth. 60·0, every morning).

The favourable effect of a *change of climate* is much recommended, but the only object attained is that thereby the possibility of new infections are avoided.

The treatment of the *hæmaturia* is the same as for cystitis. Tannin, uva ursi, buccu, chlorate of potassium, salicylic acid, oil of turpentine, balsam of copaiba, &c., are administered internally. Moreover, the bladder may be washed out with weak antiseptics and astringents. This method, however, must be used with care, as the bladder, in this disease, is very sensitive (Sonsino). A light, non-irritative diet (milk), the avoidance of spices and alcohol, and plenty of liquid (water, tea, alkaline mineral waters) are indicated.

Vesical calculi and *urinary fistulæ* require surgical treatment. When the bladder is severely affected, even without stone, Mackie has seen favourable results accrue from cystotomy.

Excrescences of the rectum should be extirpated, and in excrescences of the *female generative organs* extirpation and, or removal by, scraping, are also recommended.

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[1] Allen advises injections of saturated alcoholic solutions of santonin, and Harley injections of extract of male fern.

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IV.

THE MEDINA WORM.
(DRACONTIASIS.)

SYNONYMS.

THE parasite originating this disease is known by several names, of which the following may be quoted : *Medina worm, Guinea worm, Filaria medinensis* (Gmelin), *Filaria dracunculus* (Bremser), *Filaria æthiopica* (Valenciennes), *Dracunculus Persarum* (Kämpfer), *Dracunculus medinensis* (Cobbold), *Furia* (Modeer), *Gordius medinensis* (Linné), *Dragonneau, Ver du Sénégal, Draad, Guineesche Draakje* (Holland), *Cule brilla* (Portuguese in America), *Farentit* (Arabia) *Pejnnk* (Persia), *Irschata* (Bucharest), *Naramboo* or *Nurapoo Chalandy* (India), *Sunguf* (Senegal), *Umpha* (Dagomba), *Krukunu* (Brawa).

HISTORY.

The history of the Medina worm disease extends back to quite remote times. Joachim[1] is even of opinion that the sep-worm mentioned in the Papyrus Ebers, which, at the latest, dates back to 1550 B.C., refers to the filaria medinensis, and Bartholin and Küchenmeister believe that the fiery serpents with which the Lord afflicted the children of Israel during their stay near the Red Sea in the fortieth year of their exodus (4th Book of Moses, chap. xxi.) were no other than these worms.

The first positive statements, however, regarding these worms are found in Plutarch, who, on the grounds of a communication made by Agatharchides of Knidos, a tutor of Ptolemæus Alexander (about 150 B.C.), relates " that the people by the Red Sea suffered from a severe disease, in which small snakes—δρακόντια μικρά—came out of the skin and gnawed arms and legs, and when touched (on their appearance out of the skin) drew back again and caused the patients insufferable pain." The Greeks called the worm δρακόντιον, from which the Roman doctors originated the word dracunculus. The worm is also mentioned by the Arabian doctors.

Galen's erroneous idea that in dracontiasis it was a question not of an actual worm, but of a disease of the veins similar to the varices, was fateful to the history of the disease, for his opinion prevailed amongst medical men until the commencement of the nineteenth century, although many doctors and naturalists of the seventeenth and eighteenth centuries, such as Welsch, Kämpfer, Lind, Gallandat, &c., had confirmed the parasitical nature of the disease.

Die Heilkunde der alten Aegypter nach dem Papyrus Ebers. Verh. des x. inter. med. Kongr., Berlin, 1890, vol. v., 16 abt., p. 40.

GEOGRAPHICAL DISTRIBUTION.

The guinea worm disease is met with almost exclusively in *tropical regions*, and especially the Eastern hemisphere ; in countries where it prevails, however, it is confined to *narrowly circumscribed* districts.

The *West Coast of Africa*, from Senegal to Cape Lopez, is one of the principal centres, and there a few localities in the Gold Coast and Slave Coast are most pronouncedly visited.   On the Slave Coast, indeed, according to Siciliano, almost half the population are said to be afflicted with the parasite.   The disease, moreover, is endemic in the *Soudan* (Suard), in *Darfur, Cordofan, Nubia ;* in lower Egypt the cases observed are imported from the Soudan and the *Coast of Abyssinia.*

In *Asia* the regions of distribution of *dracontiasis* are isolated spots along the coasts of *Hedschas* (Medina) and *Jemen, Arabia Petræa, Syria* (Bay of Scanderoon), the *coasts of the Persian Gulf* and of the *Caspian Sea*, a few districts of *Turkestan* (Chiwa, Buchara, Kokan), also in *the Sir-Darja* (Kirgis steppe), and in *British India*, where the disease is endemic on the northern part of the west coast from Bombay to Cutch, the Mewar and Marwar districts of Rajputana, and the western district of the Deccan.   In the Indian archipelago, on the other hand, it is only observed in African soldiers and in Europeans who had resided for a time on the West Coast of Africa.   On the *Fiji Islands* it occurs amongst the natives.

The disease has been carried to *America*—to Guiana, Brazil, and the Antilles—by negroes from the West Coast of Africa, but has again disappeared since the importation of negroes has ceased.   It has, however, established a firm footing in isolated spots, such as the Island of *Curaçao, Demerara, Surinam*, and a few districts of *Brazil*, where it is endemic in the small township of Feira de Santa-Anna, in the province of Bahia.

In the Russian district of *Twer*, according to Cholodkowski,[1] there exists a still unclassified *filaria*, several inches in length, which causes ulcerations on the hands in the vicinity of the fingers, and is found on incising the ulcer.   Occasionally it causes extensive inflammations and even gangrene of single phalanges of the fingers.

NATURAL HISTORY.

The Medina, or guinea worm, belongs to the *Nematodes*.

The adult female (see fig. 36) is a yellowish-white, filamentous, cylindrical worm, narrowing off gradually to the posterior end, which in form and appearance resembles a violin-string.   Its length, according to Leuckart, averages from 60—80 cm., and its breadth 0·5—1·7 mm. ; in Africa, however, far larger specimens are observed, 6 feet and more in length, so that Manson is inclined to the opinion that it is a question of not one but of several species of worms.   The outer covering of the worm consists of a firm but very elastic cuticle ; it is said, indeed, to be so elastic that one may stretch it to more than double its original length. Perhaps this may be one reason why the statements as to the length of the worm vary so considerably.   The head-end (see fig. 37) is rounded off and terminates in an oval, somewhat uneven, shield-like disc in the centre of which there is a small triangular oral aperture.   At the dorsal and ventral edges of the oral aperture a small papilla rises, and six smaller ones are observed in the circumference of the shield.   These papillæ are

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[1] Wratsch, 1896, No. 3 ; Ref. Cbl. f. Chir., 1896, No. 21.
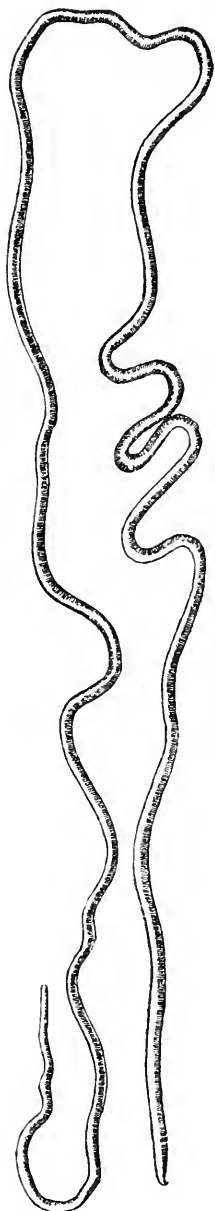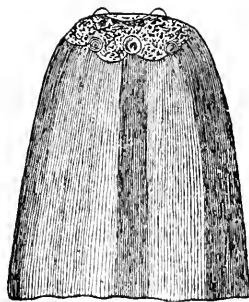
FIG. 37. — Head end of the Guinea Worm. After Leuckart.
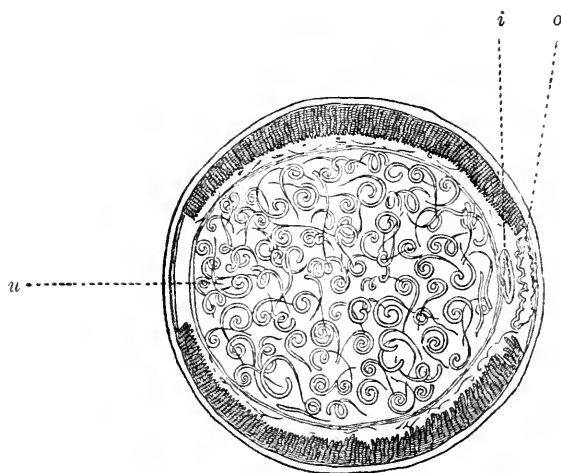
FIG. 38.—Transverse section of the Guinea Worm 5 cm. from the head end. After Leuckart. *u*, uterus with embryos; *i*, intestinal canal; *o*, ovary.

FIG. 36.—Guinea worm. After Leuckart.

considered to be organs of sense. The caudal extremity is short and curved in ventrally. The straight intestinal tract commences at the oral aperture, runs through the entire length of the worm, and terminates blindly near the tail. The principal bulk of the body is occupied by a hugely developed uterus in the form of a straight canal, entirely filled with embryos, the number of which is computed at from eight to ten millions (see fig. 38). A small shrunken ovary is situated at either end of the uterus ; neither vulva nor vagina is to be seen.

The *male* has hitherto only been observed once. In dissecting a body in Lahore, Charles discovered two female guinea worms in the subperitoneal tissue ; to each a smaller worm, about 4 cm. in length, was attached with its posterior end at a spot about 14 cm. distant from the head-end of the female. It therefore may be concluded that the male, as in *syngamus trachealis*, was seated on the vulva of the female, and that it dies off after coition, while the vulva becomes atrophied (Braun).

The *subcutaneous cellular tissue* and the *cellular tissue between the muscles* (especially of the lower limbs) is the principal *seat* of the guinea worm. Immature worms are also incidentally found in the subperitoneal tissue.

The guinea worm also infests animals such as the ox, horse, dog, leopard, jackal, canis lupaster, &c.

It has hitherto been believed that no genital pore was present in the adult worm, and that the embryos were released through the rupture of the parent organism, after it had left or been removed from its host. Lately, however, Manson has demonstrated that this view is erroneous. According to Manson, the *birth of the embryos* takes place in the following manner :—When the embryos have become mature the worm bores a hole in the deeper layers of the skin, without, however, perforating the epidermis. In consequence of the inflammation caused by the process or, it may be, through the ejaculation of an irritative secretion, a vesicle forms on the spot in question. The contents of the vesicle become opaque, and it bursts in a few days, and a round erosion or ulceration, the centre of which is cavernous, ensues.

The head of the worm is not immediately visible in the orifice, and days or even weeks may pass before it is protruded. If a little cold water is dripped on the skin near the ulceration, a drop of liquid, which is at first clear, but which afterwards becomes grey and viscid, is exuded and found to contain an enormous number of embryos. If the experiment be repeated shortly afterwards there will be no effusion, but after an hour or two it takes place again. At other times, after the trickling of the cold water, a thin, tense cylindrical rod is projected, which is seen to contain a liquid which at first is clear and afterwards becomes opaque and milky white. After a few seconds the rod bursts, and its contents, consisting of embryos, are evacuated, whereupon the rod contracts. This, according to Manson, ensues because, in consequence of the contraction of the cutaneous muscles, the uterus is forced forward through the oral aperture, which has become useless for the nourishment and movement of the worm. During the birth of the embryos the worm gradually becomes shorter, so that before the commencement of the process the worm is considerably longer than it is subsequently ; this furnishes a further reason for the diverse statements as to the length of the worm. Manson's observations coincide in the essential points with those of Forbes made sixty years previously.

The *embryos*, without decidua (see fig. 38, p. 381), are not cylindrical

in form, but are distinctly flat (Robin) and possess a long awl-shaped tail of nearly a third of the total length, which averages 0·6—0·7 mm., with a breadth of 0·01 mm. They are provided with a three-lipped mouth, a digestive canal which, according to Manson, ends blindly, but according to Bastian terminated in a slit-shaped anus, and they have two small sacci-form organs that open into the part at the commencement of the tail.

The embryos can live in water for six days, and much longer, at least fifteen to twenty days in dirty water or moist earth (Manson). If desiccated to a certain degree, they may be brought to life again by being moistened with water.

According to the observations undertaken by Fedschenko at the instigation of Leuckart, and which have lately been confirmed by Manson, the embryos that have become free and reach the water insinuate themselves into the abdominal cavity of a certain *fresh water cyclops (cyclops quadricornis)*, and after being here provided with a cutis they grow into *larvæ*, 1—1·5 mm. in length. The further history of development of the guinea worm has not been hitherto discovered. Experimental feedings conducted by Fedschenko on cats and dogs with infected cyclops were futile. Probably the larvæ, with their intermediary hosts, are introduced into the stomach of human beings in drinking water and there become free. In this position they probably also attain puberty and copulate. The males then die off and are evacuated with the fæces, while the females begin to travel, and at last reach the subcutaneous tissue (Fedschenko).

An experiment of F. Plehn's exhibits a simpler method of infection. He introduced the embryos of an extracted guinea worm into sterilised water, and soaked pieces of bananas in it, and then gave the pieces to two monkeys to eat. One of the monkeys died two months subsequently without exhibiting a guinea worm; the other died after eight months, and a worm 40 cm. in length, similar in every respect to a guinea worm, was found embedded in a fungoid mass in a swelling on the right thigh.

ETIOLOGY.

The disease is probably acquired by drinking *polluted water*—*i.e.*, water containing the intermediate host of the parasite which is infested by the larvæ.

There are a number of recorded cases which undoubtedly confirm this method of infection, and of these I cite a few from Hirsch's work.

Ferg, in 1801, observed an epidemic of dracontiasis on a coffee plantation in Surinam, and about 200 negroes were affected by it within four or five months. Not only, however, were the field labourers attacked, but the slaves also in the house of the director were affected, though they had nothing in common with the field labourers excepting the spring of water.

Cooper reports an epidemic amongst the native troops in Secunderabad (State of Nisam) which was almost entirely confined to two companies that had drawn the water they required from one well.

Dutt treated 180 cases of the disease in a village near Warora (Central India), and all the persons affected had drawn their drinking water from a dirty well; those members of the population who had made use of other water were not attacked.

In 1849 two trade caravans on the way from Bahia to Jazeiro camped out by a little river a few miles from Feira de Santa Anna, and notwithstanding the warnings of the natives, they drank of the water (without bathing in it, however). A few months later every member of this expedition fell ill with the exception of one negro, who was the only person who had not drunk the water from the rivulet.

According to another view, the worms in an adolescent state invade human beings while they bathe or while standing in water working, or wading through ditches, &c., by penetrating *through the pores of the skin*

(sweat glands) into the subcutaneous cellular tissue. This opinion is founded on the fact that the disease, in by far the majority of cases, attacks the lower extremities (see below). Ewart, however, contends with justice that many other parasites (as to the channel of introduction of which into the human body by means of the digestive tract there is not the slightest doubt) undertake extensive journeys in the human organism, and that each parasite has its seat by predilection in certain organs and tissues far removed from the place of incorporation, such as the echinococcus in the liver, the cysticercus in the connective tissue, the trichina spiralis in the muscles, &c.

The opinion that the parasites invade the body by means of the skin is more strongly supported by Harington's observations. This author observed the disease on the backs and loins of water-carriers where the leather water sack comes in contact with the body (in one case thirteen parasites) ; on the head and neck of one man who was in the habit of carrying water in a clay pitcher on his head ; and in the loins of a man who fetched a dead bird out of a pond into which it had fallen, and who continued to wear his loin cloth without drying it.

The *period of incubation* averages nine to twelve months. Occasionally, however, the time elapsing between the infection and the outbreak of the disease, may be as long as two years.

The *guinea worm* occurs in all *races* and *nationalities*, all *occupations* and *ages*, and in the male as well as in the female *sex*.

If it appears more frequently in negroes and other natives than in Europeans, and in labourers, private soldiers, &c., more frequently than in persons living under more favourable conditions, and in the male sex more frequently than in the female, the sole reason is that the classes most affected expose themselves more frequently and more recklessly to the infection than those in better circumstances (Hirsch).

Dracontiasis in certain *seasons* appears with peculiar frequency. In nearly all the countries where it is endemic (West Coast of Africa, Arabia, India) it is the rainy season and the hot season following it that yield the most cases of disease. Of course the rainy season occurs in different months, according to the geographical position of the place. In some years the disease amounts to an *epidemic*. According to isolated reports, epidemics occur in the years following those in which copious rains have fallen ; the incubation, it must be inferred, taking place in these wet years. According to Ewart, on the other hand, the frequency of the disease is in direct ratio to the quantity of rain that has fallen in the previous year, dry and hot weather particularly favouring the infection.

The geological character of the soil appears to exercise no influence on the occurrence of the disease. In former years it was sought to connect it with volcanic soil.

SYMPTOMATOLOGY.

The signs and symptoms which the Medina worm generates are usually very simple, being merely those of a local *boil-like inflammation* on the skin.

It is seldom that the wanderings of the worm cause any sensation. At the spot, however, where it will ultimately make its appearance, a dull feeling of heaviness and fulness, itching, burning, dragging or sensitiveness may set in days or weeks previously and finally increase to more or less intense pain, while an inflammatory swelling, varying in size from a filbert

to that of an egg, appears on the affected limb and prevents its use. The growth of the swelling is occasionally accompanied by fever, rigors, head-aches, abdominal pains and symptoms of colic, nausea, vomiting, an un-bearable sensation of irritation all over the body, with, in some cases, delirium and convulsions. Occasionally, when the swelling, on account of its size—and more especially if it contains several filariæ—exercises pressure on the under-lying blood vessels—stasis and œdema may set in. A vesicle soon forms on the swelling and it contains a liquid which at first is clear, but later on becomes opaque and purulent. After a few days the vesicle bursts, so that a round ulceration with a central aperture ensues, in the depths of which after a few days the head of the worm becomes visible. Sometimes the aperture re-closes, and then a second vesicle, not far from the first, forms within a few days. This likewise bursts and permits a part of the parasite to become visible. In rare cases large abscesses appear, from which, after opening, a young coiled up worm is evacuated.

When the anterior part is extruding from the aperture it is generally customary to drag the whole worm gradually out. This is accomplished by means of a slight pull two or three times daily, and in order to prevent the parasite slipping back the protruding part is usually fixed in a split stick, around which the extracted portion of the worm is wound, and then fastened over the wound by adhesive plaster or some such means. If the worm is not torn it may be extracted in this manner in from ten or twelve days, when the part soon heals. The extracted worm is usually dead, frequently shrivelled up as if mummified (Fedschenko), and contains only a few embryos, which are likewise dead (Manson).

If, however, the worm is broken during extraction the consequences may be serious, on account of the irritation set up in the surrounding tissues by the embryos expelled from the torn parasite (Davaine). In these cases severe symptoms of inflammation are set up which, under some circumstances, lead to deep-seated inflammation, periostitis of those bones along which the body of the worm extends, necrosis of the bones, putrefaction, gangrene, and even death in consequence of septicæmia.

If the worm be left unmolested its uterus gradually empties in the manner described above (p. 382), its body shrivels, and, according to Forbes, it comes out spontaneously after fifteen to twenty days from its first appearance, or may be easily extracted without danger of rupture.

The Guinea worm appears most frequently on the *legs*, especially in the vicinity of the ankle. Aitken compiled 930 cases from Indian reports, and in 98·85 per cent. of these the lower extremities were affected. In rare instances the arms, trunk, scrotum, penis, head, neck, conjunctivæ, orbit, nose, lips, and sub-lingual regions become the seat of the parasite.

Innes communicates a case in which a Guinea worm in the course of its travels invaded a *knee-joint* and originated purulent inflammation in it; after incision, irrigation, and drainage, however, it healed quickly. Williams observed two cases of synovitis of the knee-joint in persons suffering from Guinea worm without the presence of the worm being found in the joint.

Esprit publishes an interesting case. A Spahi, who had been in Senegal for years, exhibited a swelling in the cellular tissue of the scrotum, which had developed within a few weeks, and was of a nodular and lobulated character. After incision a little thin, sero-sanguineous fluid exuded. The swelling subsequently became smaller, but did not quite disappear. The mass was therefore excised. It was found to consist of retiform fibrous tissue, in which numerous little whitish bodies, varying in size from the head of a pin to a grain of corn, were embedded. All these little objects could be distinguished as *embryos* of filaria medinensis in various stages of development. Four years previously the man had had a similar swelling on the same spot, and about six weeks after his apparent recovery two Medina worms had broken through the skin, one in the

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leg, the other in the inguinal region. On this occasion the patient had not observed the presence or rupture of an adult worm. Esprit is of opinion that the embryos did not reach the scrotum by way of the blood, but directly invaded the tissue, and that the parent, after expelling them, either left its host unobserved, or had died off and become absorbed.

It is seldom that more than one worm is present in the body; occasionally, however, two, three, ten, or even more, may be present. Pouppée-Desportes observed fifty worms in one case.

DIAGNOSIS.

The diagnosis of dracontiasis, when the worm has caused ulceration and a fistulous tract, is usually quite easy.

PROGNOSIS.

The prognosis of the disease is favourable as a rule.

PROPHYLAXIS.

In districts where the Guinea worm is endemic, the *use of boiled or carefully filtered water* is the one essential preventive measure. Moreover, Manson with justice asserts that, in order to prevent a further spread of the disease, patients should be prohibited from washing their utensils in, or in the vicinity of, water used for drinking, so that the embryos that are exuding cannot drop in. The embryos should be thoroughly destroyed.

TREATMENT.

The gradual extraction of the worm, which hitherto has been the usual proceeding, should be rejected in consequence of the dangers arising from the rupture of the parasite, and because it finally comes out spontaneously. It is only when the uterus has been emptied that careful attempts at extraction are permissible. The emptiness of the uterus may be recognised by the shrivelling of the worm, and by the fact that Manson's experiment (p. 382) is no longer successful. In order to accelerate the evacuation of the uterus, Manson recommends that the legs be irrigated with cold water two or three times a day, or that the patient be ordered to take frequent cold baths. In the intervals simple water compresses should be applied. After the removal of the worm the ulcer should be dressed antiseptically.

According to Fisch, the exodus of the parasite may be considerably accelerated and eased by *massaging* the vicinity, first gently and then gradually more thoroughly. He states that by these means the entire worm may be pulled out at one sitting without causing much pain.

Various methods of killing the parasites *by internal or external means*, in order to accelerate and ease its expulsion, have also been advised. Horton and Fox for this purpose recommend *assafoetida,* taken internally. C. Forbes recommends *sulphur præcipitatum* (every four hours for the first ten days, twice daily the next ten days, in the form of Garrod's sulphur tablets = 0·3).

Fisch advises *inunction* with unguentum hydrargyri (a portion the

size of a pea daily). Emily recommends injections of a 1 per cent. solution of sublimate into the swelling caused by the worm, which by this method is supposed to be killed and absorbed in a few days. If the parasite already protrudes the sublimate is to be injected into it direct, or into the fistulous aperture, when the worm may be easily extracted on the following day.

The favourable effect of injections of sublimate have been fully confirmed. Foulkes advises injections into the worm of *alcohol* coloured by fuchsin, the idea being to harden it and thus facilitate its extraction. The addition of the fuchsin serves to show how far the worm is injected and hardened. Tufnel advises that cotton wool, steeped in *pure carbolic acid*, be pushed into the sinus with a probe, or that a probe covered with carbolic oil be introduced. Roth advises that the sinus be split on a grooved director and then bandaged with lint dipped in carbolic acid (1 : 15). The bandages should be renewed every twenty-four hours. After the second or third bandage the worm, as a rule, comes out. Finally, Faulkner states that he has drawn out the worm within an hour by the application of the *constant current* (direct contact with one pole of the battery).

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V.

FILARIAL DISEASE.

DEFINITION.

A GROUP of endemic and seemingly heterogeneous diseases occurring in tropical and sub-tropical countries are comprehended under the term *filarial disease* (*Filaria-Krankheit, filariasis, filariose, maladies filariennes*). These diseases occur in the lymphatic system and are attributable to the presence of a parasite, *filaria Bancrofti*. Under this head hæmato-chyluria, elephantiasis (Arabum), lymph scrotum and various other forms of lymph-angiectasis and lymphorrhagia are included.

HISTORY.

In 1863 Demarquay, in Paris, made the discovery that the fluid from the hydrocele of a Havanese emptied by puncture contained microscopic round worms, the embryos of a nematode. Three years later they were found by Wucherer, in Brazil, in the urine of a patient suffering from hæmaturia. In 1868, without having had any knowledge of these discoveries, Lewis in Calcutta observed the same parasites in the urine of a patient suffering from chyluria, and two years afterwards in the blood of a patient suffering from chronic diarrhœa. Lewis subsequently found the parasites not only in the blood, but also in the lymphatic secretions of persons afflicted with elephantiasis-pedum or scroti, and likewise in the blood of hæmaturic people. Lewis, from his observations, came to the conclusion that these were not accidental coincidences, but that the different diseases were related and were dependent on the presence of this hæmatozoon, to which he gave the name of *filaria sanguinis hominis*. Lewis' discoveries were, later on, confirmed by many observers.

The knowledge of the ailments originated by the parasites was, partly at least, very ancient. The Arabian doctors of the ninth and tenth centuries gave a good description of *elephantiasis* under the name of *Dâ-al fil*—elephantine disease. The Latin translators of the treatises translated this word as "elephantiasis," a term which the Greek doctors had already used for leprosy. In consequence, there was great confusion in the nomenclature, as was explained in the chapter on leprosy.

The first accounts of endemic *hæmato-chyluria* were given in 1812, when Chapotin communicated the occurrence of this disease in Mauritius.

Patrick Manson gained great distinction by his study of filarial disease in Amoy (China). He, in particular, discovered the periodical appearance of the filariæ in the blood (*filarial periodicity*, Cobbold) and studied the history of their development.

GEOGRAPHICAL DISTRIBUTION.

(SEE MAP IV.)

Filarial disease only occurs *in tropical and sub-tropical* countries, and it exists for the most part endemically along sea-coasts and on the shores of large rivers. Within these regions there are *small narrowly circumscribed centres* to which the disease is confined, while the whole vicinity,

notwithstanding similar conditions of the soil, are quite, or almost entirely, exempt.

The following places are known as the geographical region of distribution of filarial disease : *India* and *Further India, Ceylon, the Malay Archipelago, China,* especially the southern and south-eastern coast ports, *Japan,* particularly the most southern of the four great Japanese islands Kiushiu, and the neighbouring smaller islands, such as the Goto Isles, Hirado-shima, Amakusa, &c.   In the following places filarial infection is also more or less prevalent, *Egypt, East Africa* (Mombasa, Tanga, Coast of Zanzibar), *Cape Colony, Orange River Colony,* (Bloemfontein) the *West Coast of Africa* from Senegambia to the Congo, *Madagascar, Réunion, Mauritius, Australia* (Queensland), *New Caledonia,* the *South Sea Islands, Brazil, Guiana,* the *Antilles,* the *Southern States of North America.* Lately, Font has even reported a sporadic case of filarial disease in *Spain,* in the neighbourhood of Barcelona.

Elephantiasis so intimately associated with filariasis, still exists endemically in *Syria, Arabia,* on *Luzon* (Manila), in *Corea,* in the *Soudan,* in *Abyssinia,* on the *Shores* of *Lake Nyassa,* on the *Zambesi,* on the *Coast* of *Mozambique,* on the *Seychelles,* in *Peru, Columbia, Venezuela,* on the *Atlantic Coast* of the *States of Central America,* and in *Mexico.*   Although filaria in these countries has hitherto either not been observed at all, or at least is very rarely found, the fact that elephantiasis, which is caused by filariæ, prevails has been proved beyond doubt.

In some districts, filarial disease is so widely spread, that a large proportion of the population is affected by it.   In Amoy (China) according to Manson, one-eighth of the population suffer from filarial disease.   On the Fiji Islands Thorpe found filariæ in 25 per cent. of the natives, and on the Friendly Islands in 32 per cent.   In the districts of Travancore and Cochin (the southern point of India) one-tenth of the total population are, according to Underwood's official report, afflicted with elephantiasis, and according to Waring, in one district there with a population of 48,600 souls, 2,133 persons (1 : 22·7) suffer from this disease (Hirsch).   On Samoa, according to Königer, 50 per cent., of the male population have elephantiasis and in some families all the members are affected.   The Island Huahine, one of the Friendly Islands group, seems to be the most severely afflicted region known, for, according to Saville, seven-tenths of the male adult inhabitants suffer from elephantiasis.

SYMPTOMATOLOGY.

The various forms in which filariasis declares itself are—

1.   Hæmato-Chyluria.

Hæmato-chyluria occurs as a rule intermittently.   The paroxysms may be repeated throughout several weeks or months.   *Intervals* of freedom from attacks may last for months or years, during which time the urine is quite normal.   The attacks, which sometimes come on spontaneously and in other cases set in after bodily exertion, emotion, or other physical or mental excesses, are occasionally ushered in by fever, with more or less severe *pains* in the back, in the abdomen, the groins, the anterior aspect of the thigh, the scrotum and in the perinæum.

The condition of the *urine* is remarkably characteristic.   Sometimes hæmaturia and sometimes chyluria predominates.   In the former case the

urine mostly exhibits a peach-coloured tint, and is not transparent. If allowed to subside the blood sinks to the bottom, frequently as coagula, and the supernatant urine is opaque-white, with a yellowish tinge, rather like diluted milk.   Occasionally a distinctly cream-like layer is also deposited.   In other cases, especially in the later periods of the attacks, the evidence of blood is absent, and the urine throughout is milky and uniform ; but sometimes whitish, sometimes jelly-like coagula form in it, or all the urine coagulates to one loose mass, taking the shape of the utensil.

Sometimes there is formation of thrombi within the bladder itself, the consequence being temporary retention of urine, which persists until the clots have passed through the urethra, a process that causes the patient severe pain.

If the chylous urine be shaken up with ether after the addition of a little solution of caustic soda it loses its milky appearance, the fat suspended in it becomes dissolved, but the urine does not generally clear up entirely.   The quantity of fat in the urine is remarkably variable.   In one case I had under observation for months, and in which a great number of analyses were conducted, the contents with ether extract varied from 0·6 to 3·3 per cent., exceeding considerably the proportion of fat in normal serum.   Besides neutral fats and fatty acids, the urine also contains cholesterin and lecithin.   Albumen is always present, but in variable quantities.   In this particular case the quantity averaged from 0·6 to 2·6 per cent. Like other observers I could never demonstrate either peptones or sugar.

In consequence of the fatty constituents in chyluria often exceeding the quantity in chyle, and also on account of the absence of sugar, the erroneous conclusion has been arrived at that chyluria is not induced by the admixture of chyle with the urine.   The fatty contents of the chyle of a person must necessarily depend upon the composition of the food he has partaken of and on his state of digestion when he comes under observation ;   therefore isolated analyses of chyle taken from dead bodies, such as the old analysis of Rees[1] undertaken on the chyle of a criminal who had been executed, and which yielded a proportion of fat of 0·92 per cent., is not pertinent to this question.   It is better for purposes of comparison to make use of the analyses of the chyle of animals in which a far greater quantity of fat has been demonstrated.   Hoppe-Seyler[2] found 6·5 per cent. extracted by ether in the chyle of an ox.   Moreover, it must be taken into consideration that it is very difficult to abstract a sufficient quantity of chyle for analysis from anywhere but the thoracic duct, and therefore it is usually taken from thence ; the amount of fat in the contents of the vessels of the lymphatic system, however, always decreases in amount as we proceed from the peripheral to the central vessels and the thoracic duct.   According to an old analysis of Tiedmann and Gmelin[3] the chyle of a horse taken from the mesenteric glands exhibited 9·03 per cent. of fat, proximally to these glands 1·23 per cent., and from the contents of the thoracic duct only traces of fat were found.

In regard to the absence of *sugar* from the urine of sufferers from chyluria, this is not surprising according to v. Mering's investigations.   This author, through experiments made on animals, demonstrated that the lacteal vessels take no essential part in the absorption of sugar from the intestine, the absorption principally taking place through the intestinal veins.   He found no more sugar in the chyle than in the blood serum and in the lymph (0·1 to 0·2 per cent.), and therefore concluded that the sugar in the chyle originates from the blood.   When chyle is mixed with urine the sugar in the latter must therefore be diluted to such an extent as to become undemonstrable by means of the usual methods.   This is sufficient explanation of the negative results obtained in the search for sugar in the urine of chyluria patients.

The *microscopic examination* of the urine shows the presence of delicate, dust-like particles of fat.   If the fatty elements are in larger quantity the particles of fat are likewise larger.   Red and white blood corpuscles are

[1] *Philos. Transactions*, 1842, p. 81.
[2] Physiologische Chemie, 1881, p. 595.
[3] v. GORUP-BESANEZ.   Handb. der phys. Chemie, 2nd edition, 1867, p. 370.

also found in variable quantity, and frequently, but not constantly, the *embryos* of *filariæ*, to be described below.   In uncomplicated cases urinary casts are never observed.

The re-action of chylous urine is usually faintly acid.   The specific gravity is sometimes increased, sometimes diminished, being mostly decreased when it contains much fat.   The quantity of urine passed in twenty-four hours does not generally deviate essentially from the normal.

The quantity of blood and fat in the urine varies not only on different days, but at different times of the same day.   At one time the urine passed early in the morning is richest in blood, and contains the most numerous filariæ, at another time this condition is exhibited in the urine passed later on in the day.   The afternoon urine is usually the most chylous, whereas the urine passed in the morning and at night shows the smallest quantity of fat.   Bodily movements and meals cause the admixture of abnormal constituents to be increased.   If much fat is partaken of, the urine exhibits more fatty ingredients.   After repeated aperients, Lancereaux observed that the chyle in the urine almost disappeared.

Towards the termination of the attacks, the urine generally regains its normal condition, but traces of albumen are often left after apparent recovery.

Occasionally the hæmato-chyluria does not set in paroxysmally, but runs a continuous course.   I saw one patient who had been uninterruptedly affected for two years.

The disease may extend over many years without essentially weakening the constitution.   The patients may attain a great age, and then succumb to another disease.   In other cases, on the contrary, anæmia and emaciation gradually set in, and the sufferers often perish, after exhausting diarrhœa has appeared as a concomitant.

Hæmato-chyluria is observed more frequently in the *coloured races* than in whites, the former being less careful in their choice of drinking water than the latter ; it is especially a disease of *middle age*.   According to Lewis, *women* are more frequently attacked by the disease than men, and Manson also is of opinion that the female sex is the more liable.

In women, pregnancy and parturition are *predisposing causes*, and in men running and jumping.

On the Friendly Islands the *chiefs*, according to Thorpe, are *more rarely* attacked by filariasis than the lower classes, being much more careful in their choice of drinking water.   The drinks in these islands consist of cocoanut milk, and kava (the juice of the chewed roots of piper methysticum mixed with water).

2.   Elephantiasis Arabum.

Synonyms : *Elephantia, Elephantopus, Bucnemia*[1] *tropica* (Mason Good), *Pachydermia* (Fuchs), *Spargosis fibro-areolaris* (Wilson), *Hypersarcosis* (Kämpfer) *Sarcoma mucosum* (M. Aur. Severinus), *Barbados-leg, Cochin-leg, Mal de Cayenne, Roos-been van Suriname, Fe-fe* (Samoa), *Pejäht, i.e. :* insects within (Siam).

Elephantiasis consists principally of hypertrophy of the cutis and subcutaneous tissues.   It is mostly situated in the *lower extremities* and the *genitals*—in men in the scrotum and penis, and in women in the labia pudendi, the clitoris, the mons veneris, and the inguinal region.   In the inguinal region, sometimes pendulous, pedunculated elephantoid masses are observed (Daniels).   The upper limbs are more rarely affected.

In exceptional cases other parts of the body, such as the mamma, ear

[1] Derived from $\beta o \nu \ldots =$ (in compounds) large, monstrous, and $\chi \nu \eta \mu \eta =$ leg.

lobes, head, and buttocks are diseased. In British East Africa, Kolb once observed elephantiasis of the tongue, which protruded sausage-like about 20cm. from the mouth, the lower jaw also being enlarged. The disease is confined usually to one of the lower extremities, the leg and foot being most severely affected.

According to Manson it is remarkable that in the *South Sea Islands* the *arms* and *breasts* most frequently become attacked.

The disease mostly, if not always, develops with symptoms of *lymphangitis*, which, accompanied by fever, return at irregular intervals of weeks, months or years.

The attacks usually commence with severe rigors, followed by high fever, with head-ache, prostration, thirst, vomiting and delirium. The temperature rises to 40° or 41°. Red streaks appear on the skin which, singly or in larger numbers, advance upwards on the limbs, and are very sensitive on movement, or to the touch ; the lymphatic vessels can be felt as tense cords interrupted by harder nodules. The lymphatic glands swell and become painful, and the skin over them is tender and swollen. After one or two days, a profuse perspiration breaks out accompanied sometimes by the exudation of a lymphatic or chylous liquid from the diseased part, and the inflammation then disappears. Occasionally, after feeling relatively well for a few hours, a second attack sets in, and this may be repeated several times. At times an abscess forms, or the diseased parts become gangrenous, and death may even result in consequence of blood-poisoning.

Attacks of fever of this kind (elephantoid fever, filarial fever), which used formerly to be mistaken for attacks of intermittent fever, occur, not only in elephantiasis, but in the other forms of filarial disease still to be mentioned, and when the seat of disease is invisible may go on without perceptible symptoms of inflammation. The attacks of fever are not rarely induced by incidental causes, of which the most frequent are chills, bodily exertions, standing a long time, and, above all, by external injuries and irritation, such as the rubbing of the scrotum against the thighs, scratching in consequence of scabies, the stings of insects, erythema, injuries from pointed or sharp stones, the thorns of plants, &c.

Perhaps the severe *forms of erysipelas* mentioned above as occurring in Brazil and Réunion may, at least in some instances, be due to filarial disease.

After every attack of lymphangitis the swelling of the skin decreases, but a gradually increasing œdema is left behind. The skin gradually becomes thicker and more tense and firm. Its surface is either smooth (*elephantiasis glabra, lævis*) or covered with warts and protuberances (*elephantiasis verrucosa, tuberculosa*). In consequence of the thickening of the epidermis the formation also of ichthyotic masses may take place. Pigmentation is often observed, and excoriations may ensue, from which ulcers with callous borders develop.

Should the disease affect one of the *lower limbs*, the leg is found to be enlarged to twice or even thrice its usual dimensions. It resembles a huge cylinder which, the constriction and folds at the ankle joints being entirely obliterated, joins the thickened dorsum of the foot continuously, resembling actually an elephant's leg. The circumference of the limb in the region of the ankle may average 60 cm. and more.

The hair grows irregularly on the diseased limb and is very coarse ; the nails are thickened, rough, and misshapen ; the sensibility is somewhat diminished.

The *scrotum* (see table V., fig. 39) becomes a monstrous pedunculated mass, reaching from the inguinal regions, it may be, to the knees or even to the ankles, and the penis completely disappears. In other cases the penis participates in the disease, and either becomes uniformly thickened and enlarged or becomes quite misshapen and unrecognisable. Weights of 20 to 30lbs. (in the case illustrated the weight was 32lbs.) are not unusual in these scrotal enlargements. Clot Bey operated on a patient whose scrotum weighed 110lbs. The largest tumour ever removed is mentioned by Chevers,[1] and was said to have weighed 224lbs. In most cases large hydroceles are present in the scrotum. When the scrotal tumours are large, abscesses may form or gangrene may occur.

The *female genitals* (*see* table VI., fig. 40) may be transformed into similar protuberances by the disease, and may reach to the knees or even below them.

The *inguinal glands* as a rule enlarge and become prominent, hard tumours, which are sometimes divided into two masses by Poupart's ligament. In elephantiasis of one leg the inguinal glands of both sides are often enlarged.

Subjectively the patients are mostly only troubled by the *deformity* and *weight* of the diseased member which, as we have seen, may be so considerably enlarged as to impede or prevent all locomotion.

Elephantiasis principally occurs in the *coloured races*, and it is amongst the section of the population living under unfavourable conditions that the disease prevails. The coloured races, as already mentioned, are less careful in the choice of their drinking water than white people, and the working classes are particularly exposed to the incidental causes that induce the lymphangitis that leads to elephantiasis, a condition to which their lack of clothes materially contributes. When whites live under the same conditions as the natives, they appear to be liable to the disease in the same degree.

The disease is more frequent in the *male sex* than in the female.

As to the *age* at which it appears, elephantiasis has never been observed in children under ten years of age, it is excessively rare up to the twentieth year of age and increases in frequency with every decade. In old age, however, the primary manifestations are absent.

Moncorvo, senr. and junr., in Brazil frequently observed *congenital elephantiasis* and also *acquired elephantiasis* in *early childhood*. In congenital elephantiasis, however, they never found filariæ, but always the cocci of erysipelas.

3. Lymph Scrotum.

Lymph scrotum is nearly related to elephantiasis scroti, of which it may be but the precursor. Redness and swelling of the scrotum set in, accompanied usually by symptoms of fever; vesicles and blebs, from the size of a pin's head to a finger-tip, form on the scrotum and finally burst, discharging their fluid contents. Such attacks, although at first not frequent, occur more and more often later on, so that at last the fluid is discharged continuously and may amount to several pints in the twenty-four hours.

The fluid excreted is either as clear as water or it is milky, or it may be sanguineous and coagulate on exposure to the air. The microscopic examination of the fluid almost always reveals *filarial embryos*, though

[1] "Diseases of India," p. 269.

PLATE VI.

Fig. 40.
ELEPHANTIASIS OF THE RIGHT LABIUM PUDENDI AND THE SUB-INGUINAL REGION
in a Japanese woman.

they may be absent from the blood.   Manson once found *eggs* in the fluid of the discharge.

The scrotum feels soft, with a jelly-like elasticity ; it is sometimes smooth, but more often wrinkled, and on incision it is observed that the tissue is interspersed with spaces and recesses filled with lymph.   The testicles may be enlarged, and hydrocele of one or both sides may be present.   The groin glands, as a rule, are enlarged.

Lymph scrotum is frequently combined with elephantiasis scroti ; in the same way that an elephantoid leg may be occasionally accompanied by lymphorrhagia.

The disorders of the patients partly depend on the weight of the tumour and partly on the drain on the system due to the quantity of lymph excreted.

4.   Varicose Groin Glands.

Varicose groin glands are observed more frequently in men than in women, and may occur in addition to the other forms of filarial disease, or they may be the only evidence of filarial infection.   Varicose groin glands are distinguished by a bulging, soft, doughy, half-fluctuating enlargement as large as a fist in which hard nodules may be felt here and there, and over which the skin is unchanged.   The swelling may occasionally be removed by pressure, but it returns as soon as this is relaxed.

According to Manson, a *femoral* and *inguinal* enlargement may be differentiated.   The former is situated in the region of the cribriform fascia, and is usually of an oval shape, the long axis of which is in a vertical direction.   The inguinal enlargement, which is usually the larger, follows the course of Poupart's ligament, and in well-developed cases may extend from the region of the iliac spine to the pubes.   As a rule, both groups of swellings are present, but one occasionally finds either the inguinal or femoral alone affected.

Occasionally varicose, dilated, lymphatic vessels are found in the vicinity, and these occasionally reach as low down as the popliteal space ; in such cases lymphorrhagia is frequently observed (Mazaé Azéma).   The lymph vessels of the vas deferens may also become varicose.

Clear, milky, or sanguineous fluid may be drawn off from the varicose lymph glands by means of a Pravaz's syringe ; this fluid under the microscope almost always exhibits filaria embryos and, in rare cases, ova. The groin glands on both sides are usually affected, and except during the periodical attacks of lymphangitis, they are not painful; but after long-standing, severe bodily exertion, especially during very hot weather, the glands enlarge, and cause a strained or dragging sensation.   In women the glands become enlarged during menstruation and pregnancy (Mazaé Azéma).

Should elephantiasis follow, the soft swelling is transformed into a hard tense mass.

In rare cases other lymphatic glands, particularly the axillary glands, may become similarly diseased.   Bancroft designated the varicose groin and axillary glands *helminthoma elastica*.

5.   Rarer forms of Filarial Disease.

Lymphatic varix, without the accompaniment of varicose lymphatic glands, are occasionally found on various parts of the body, such as the

abdomen, legs, arms, &c. *Varices of the lymphatic vessels of the vas deferens* likewise occur alone. The latter have some similarity to varicocele, but are differentiated from this by their feeling softer and by the dilatation of the lymphatic vessels being more unequal than that of the veins.

A form of *orchitis* occurring in some filaria countries also appertains to filarial disease. It commences suddenly with symptoms of fever of the character described above. The testicle, accompanied by severe pain, swells quickly to three or four times its original size. The epididymis and the vas deferens participate in the inflammation, and a clear or milky effusion is discharged into the tunica vaginalis. Sometimes, also, the surface of the scrotum exhibits a slight inflammatory swelling. When the fever disappears the pain rapidly diminishes and the swelling gradually subsides. If the effusion into the tunica vaginalis is clear, absorption of the fluid usually takes place. A chylous effusion, on the other hand, is not usually reabsorbed, but develops into a chylocele. Attacks of this kind are repeated at longer or shorter intervals, and are at times accompanied by other filarial symptoms.

A form of *chylocele* occurring endemically is to be classed with these forms of filariasis. It either develops gradually or is an outcome of the orchitis described above. The chylocele seldom attains a large size. According to Magalhães it is, as a rule, least tense early in the morning and seldom attains the tension presented by the ordinary serous hydrocele. It is also distinguished from the latter by the fact that it is not translucent. The effusion in the tunica vaginalis has a milky or pale-red appearance, and, according to Manson, sometimes contains an enormous number of filariæ, either living or dead. The number of filariæ present is far greater than in the lymph obtained from varicose groin glands or lymph scrotum.

Filarial disease may perhaps also contribute to the formation of *chylous ascites*. Many observers, amongst them Manson, are of opinion that the frequently quoted case of Winckel was of this nature. According to my opinion, however, this view is erroneous, for the round worms found in Winckel's case differed considerably from filaria embryos ; moreover, according to my information, there are no reports as to the endemic occurrence of chylous ascites from the countries where filarial disease is endemic.

Winckel's case related to a missionary, 39 years of age, who had lived in Surinam for nine years. Two litres of a milky-like fluid were removed from the abdominal cavity by means of tapping. The ascites had been present for three years. Filamentous organisms possessing lively mobility and which had *several cilia on the head-end* but no *mantle-like* sheath, were found in the fluid. They were 0·2 mm. in length and 0·01 in breadth. No swelling could be felt in the abdomen of the patient ; the urine was normal ; the blood was not examined. Death occurred four years later after a second removal of nineteen pints of similar fluid. No autopsy was made.

When sanguineous and chylous material are present in the stools it is possible that the accompanying diarrhœa has some relation to filarial diseases.

Lewis mentions a case of chyluria in which a copious white fluid flowed from the *conjunctival* surfaces of both eyes, which were trachomatous and leucomatous. Filariæ were found in the blood, in the urine, and in the tears, which undoubtedly originated from dilated lymph-vessels.

In filarial patients the appearance *of abscesses*, superficial as well as deep, are by no means of rare occurrence. Although such abscesses may be the result of ordinary inflammatory processes, they sometimes seem to be directly induced by the parasites, for filariæ have repeatedly been found

in the pus of such abscesses. Occasionally they exhibit a tendency to bleed (Kennard). If they are situated in the thoracic or abdominal cavity they may lead to serious disturbances. Manson is of opinion that the abscesses in many cases are, as in Guinea worm, caused through the irritation of dead parent worms.

Maitland also instances *acute synovitis* as a not infrequent complication of filariasis ; in his cases only the knee-joint was affected.

The separate forms of filarial disease may occur in one individual. Thus it is not uncommon to observe patients who are simultaneously afflicted with hæmato-chyluria and lymph scrotum; others with lymph scrotum and elephantiasis of the leg; others still, with chylocele and varicose groin glands, &c.

In conclusion, it must be mentioned that filaria embryos are frequently found in the blood of persons who are quite healthy and exhibit none of the affections described, and who are suffering from no other complaint. Da Silva Lima found that of twenty-six persons examined who had filaria embryos in the blood, twenty-one were free from any clinical signs or symptoms of the infection.

NATURAL HISTORY OF THE FILARIA BANCROFTI AND PATHOLOGICAL ANATOMY.

The *adult filaria parasite*, which belongs to the *nematodes*, was first discovered in Brisbane (Australia) by Bancroft in 1876, in a lymphatic abscess on the arm of a patient. Cobbold, out of compliment to the discoverer, gave the parasite the name of *filaria Bancrofti*.

The *female* (fig. 41), which at first alone was known, is a filamentous white worm, 85 to 95 mm. in length, and of the thickness of a human hair. The head has a round, unprotected oral orifice. The neck is thin, one-third the thickness of the body. The tail has a stumpy termination. The anal aperture is at the tip of the tail, and the sexual opening near the head. A simple digestive tract extends from the mouth to the anus. The rest of the body is taken up by the sexual organs. The uterine tubes are crammed with myriads of ova in all stages of development, which are 0·016 to 0·026 mm. in diameter. According to Manson, the filarial worm normally is viviparous, but it happens that the eggs are prematurely deposited, so that it becomes oviparous. Manson twice found ova in the lymph ; once in a case in which the lymph came from varicose groin glands, and in another case from a lymph scrotum.

The *male* is shorter and thinner than the female. Daniels gives its length as 44 mm. Its caudal end, according to Manson, is strongly curved, and possesses two uneven spicula, of which the longer has its free end turned backwards forming a hook similar to the handle of a walking stick ; whereas the end of the shorter one is direct towards the orifice of the cloaca. Pre-anal papillæ are absent, but three rudimentary pairs of post-anal papillæ can be distinguished.

FIG. 41.—Filaria Bancrofti, female. Natural size. After Cobbold.

The males and females are generally found together,

probably copulating. Occasionally the parasites are present in great numbers.

The embryos (fig. 42) which are found in the blood, urine, &c., are delicate, translucent, cylindrical and smooth, rounded at the head-end and pointed at the caudal extremity. No organs can be perceived in them with the exception of a double longitudinal streak, which is more distinct about the middle of the body and which probably indicates a rudimentary intestine. With a higher power delicate transverse markings may be perceived. For further details of the more minute structures, see below, p. 399. The embryos are enveloped in an exceedingly thin structureless sheath which closely envelops the greater part of the body, but which extends beyond the head of the parasite and particularly beyond the tail, where it sometimes appears in the form of a delicate flagellum and sometimes as a bag-like projection. Within this sheath, which is probably an embryonic integument, the embryos are observed to project themselves backwards and forwards. The movements are continuous and serpentine and the tail whips about lustily amongst the blood corpuscles. In preparations protected from desiccation the embryos may remain alive for days. They usually die in an extended or half bent attitude. After death they become more granular in appearance. As their size varies considerably, the statements of the different observers as to their dimensions do not coincide entirely. Lewis gives the length of the embryos as 0·34—0·37 mm. and their breadth as 0·007—0·008 mm. Crevaux states that their length is 0·265 mm. and their breadth 0·010 mm. I found them on an average 0·216 mm. in length and 0·004 mm. in breadth, therefore nearly corresponding to the diameter of a red blood-corpuscle, so that they are able to pass through the capillaries unchecked.
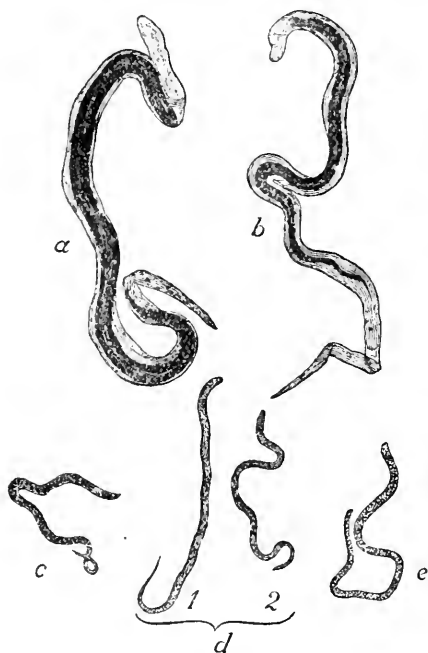
Fig. 42.—Filaria embryos, enlargement 300 times after Manson. a, Filaria nocturna; b, Filaria diurna ; c, Filaria Demarquayi; d, Filaria Ozzardi: 1, sharp-tailed form, i.e., Filaria Demarquayi, 2, stump-tailed form, i.e., Filaria perstans ; e, Filaria perstans.

The number of filarial embryos present in specimens of blood, urine, &c., varies extraordinarily. Sometimes a number of preparations have to be examined before one embryo is discovered. In other cases they are so numerous in one drop of blood, that supposing the proportionate number were equally distributed in the body the total would amount to millions. Mackenzie computed their number in one case to be from thirty-six to forty millions.

If the number of embryos is very few in the urine or the chylous fluid, it is advisable to *filter* the excretions and to use the coagulum or drops of thick fluid remaining on the filter for examination.

In order to discover the filaria in the blood, Manson recommends *stained dry pre-parations*. The blood should be allowed to dry on slides (they may be put away and kept for months in this way), and should then be stained for 1—2 hours with a weak solution of fuchsine (3—4 drops of saturated alcoholic solution to 30 g. water). If the stain is too deep, the preparations should be placed in diluted acetic acid (2—3 drops to 30 g. water) for a few minutes, and then washed through. They should be immediately examined damp and without a cover glass with a low power. The embryonal sheath does not take the dye, and is therefore hardly perceptible. Unfortunately such prepara-tions only last a few days.

In order to arrange *permanent preparations*, Manson recommends that they be fixed with absolute alcohol or by heat. They should be stained with $\frac{1}{2}$ per cent. solution of eosin, and embedded in glycerine, glue, or Canada balsam. For this, however, fresh dry preparations are necessary.

In order to preserve permanent preparations in which the *sheath* may become visible, the process is as follows: The blood, which should be spread on the slide in a very thin layer, should be dried over strong acetic acid; the slides, with blood smear downwards, being placed on watch-glasses which contain a few drops of acetic acid. As soon as the blood has dried up a few drops of solution of eosin are trickled on to it, and left for two minutes; the stained preparation is then well rinsed in water, slowly dried, and embedded in balsam. The red blood corpuscles and the serum become stained, the white blood corpuscles and the filaria, on the other hand, remain unstained, and the filaria appear of a dazzling whiteness (Manson).

De Nabias and J. Sabrazès advise a *double method of staining*. A small coagulum taken from the chylous fluid is spread on a slide and dried over the vapour of a 2 per cent. solution of osmic acid; the preparation is then passed through a flame a few times and coloured with borax-carmin (Gibbes) for a quarter of an hour. A short treatment with a mixture of one part hydrochloric acid and 100 parts of 70 per cent. alcohol, should follow; the preparation is then stained in water for twenty minutes with a concentrated watery solution of methylene blue; well rinsed, dehydrated in alcohol, passed through oil of cloves, and mounted in Canada balsam. By this method the embryos are stained blue and their sheaths pale red.

Interesting observations on the further development of filaria embryos have been published by Manson and Bancroft. The embryos do not grow to adult worms in the human body, but must leave it to develop further in an intermediary host, and then invade man anew. *Mosquitoes* —according to Bancroft, *culex ciliaris*, Linn.—play the part of the inter-mediary host, and their breeding places are formed by water utensils in and around houses.

The female mosquitoes—for the males have no sting, and do not live on blood—suck filaria embryos into their stomachs with the blood of filaria patients; and in this situation the embryos are found relatively in larger numbers than in the blood of patients. The mosquito sting, therefore, on account of its structure, must be peculiarly adapted to draw the filaria embryos from the capillaries, as with their sheaths they probably get entangled in the proboscis. Manson infers from this that the mosquito is the natural intermediary host of the filaria. Some of the embryos are digested, others, after slipping from their sheath and boring through the walls of the stomach, invade the muscles of the thorax, and here within two or three weeks and after several metamorphoses, are transformed to an actively mobile worm 1·63 mm. in length and 0·031 in breadth.

The worms are provided with an intestinal tract, a conical head, and a three-lobed caudal appendage. The latter, when dragged after the body, folds up, and thus does not check the worm in its wandering through the tissues of the host; when the tail is projected backwards, it opens out like a tripod, thus forming a powerful basis for pushing forward. Manson regards the head as well adapted to bore its way through the tissues.

Manson, in his investigations, found the filaria larvæ already fully developed six days after the mosquitoes had sucked filarial blood. Bancroft, on the other hand, only on the sixteenth or seventeenth day, in cold weather on the twentieth day, or even later, and the latter explains this difference by the fact that he used mosquitoes bred by himself, which Manson did not. It is therefore probable that Manson's mosquitoes had

sucked filarial blood some time before the actual observation, and this view is strength-
ened by the fact that Manson in his mosquitoes found filariæ in various stages of
development, which Bancroft did not.

There are at present no positive observations as to the further fate of
the filaria larvæ.

The impregnated and satiated female mosquitoes betake themselves to
the nearest stagnant pool, and there deposit their eggs and die.   Accord-
ing to Manson's opinion the filaria larvæ then become free, and if the
water is used for drinking purposes, they are thus taken into the human
stomach, through the walls of which they bore and wander about in the
body of their host till they have found a suitable seat.   They there attain
puberty and multiply by means of sexual generation.

Bancroft, who found that the larvæ could not live in water, but die in
it after three or four days, does not therefore coincide in the view that
they are introduced into the stomachs of persons with the drinking water.
He is of opinion that infection occurs through mosquitoes containing
larvæ being swallowed when they get into the mouths of sleeping persons,
or when they have fallen into food, or when they have been killed with
the hand, when portions of them may adhere to the fingers, which may
subsequently be put to the mouth.   Bancroft also considers that transmis-
sion is possible through the bite of filariated mosquitoes.

The latter inference finds a support in Low's latest investigations,[1] undertaken
under Manson's directions. Low examined mosquitoes infected with filariæ and
found parasites in their head and proboscis.

Myers' experiments to transmit filarial disease to monkeys, by giving them water to
drink in which mosquitoes, fed on the blood of filarial patients, had deposited their
eggs, gave negative results.

Manson's and Bancroft's observations find analogies in the meta-
morphoses gone through by the filaria medinensis in fresh water cyclops
(see p. 368) and the filaria recondita of dogs in fleas and a species of tick
(Grassi).   This well-known parasitologist has adopted the opinion of
Manson and Bancroft respecting the development of the filaria san-
guinis hominis, whereas Leuckart's opinion differs somewhat, inasmuch
as he believes that mosquitoes are not the only creatures in which the
parasites find the conditions necessary for their metamorphosis.   It seems
to him far more natural to conjecture that any small water animal may
serve as the intermediary host of filaria Bancrofti, and these may transmit
them to their ultimate hosts.

A long period often elapses between the invasion of the parasites in
man and the first appearance of the disease.   It has been repeatedly
observed that the complaint breaks out in people, who have formerly
dwelt in the tropics, only several years after they have returned to Europe.
The reason for this lies either in the circumstance that the filaria per-
chance require years to attain complete development, or that in such
cases they at first are situated where they are harmless to the human
organism, and only reach more dangerous localities after manifold
wanderings.

Bancroft computes the duration of life of filariæ at some years, that of
the embryos at a few months.

In regard to the *seat* of the adult parasites in the human body, these
are met with in dilated, sinuous, lymph vessels, in the thickened walls of
the vas deferens, in the scrotum and lymphatics of the cutaneous tissue.
In other cases their exact dwelling place cannot be accurately ascertained.

[1] *Brit. Med. Journal*, 1900, June 16, p. 1456.

They have been met with in (lymph) abscesses; in one case Lewis discovered them in the blood clot obtained after incision of an elephantiasis scroti. Hillis found them in the urine of a man suffering from hæmato-chyluria, in this case the urine previously had contained neither embryos nor eggs.

Czerny found a female filaria in the slightly enlarged *ovary* of a woman 40 years of age (Brazil); this fact has also been noted by Thiesing.

Figueiro de Saboia at an autopsy found a pair of filariæ in a *blood clot* of the left ventricle; they have been minutely described by Magalhães (the female was 155 mm. in length and 0·66 mm. in breadth, the male 83 mm. in length and 0·4 in breadth). No statements, however, are given by Magalhães as to cause of death, symptoms of the disease during life, &c. It seems to me, as it does to Manson, doubtful if in this case it was a question of filaria Bancrofti, and Manson therefore designates this worm filaria Magalhãesi.

Most probably the *lymphatic system* is as a rule the seat of filaria Bancrofti, and it is particularly the *larger lymphatic trunks* which they choose for their abode. The large lymphatic trunks become more or less obstructed, partly by the parasites themselves, partly by the coagulation of the lymph that takes place around the worms, and in consequence of the chronic inflammation of the lymphatic vessels set up by the continuous irritation. In consequence, an engorgement of the peripheral lymphatics is set up, the vessels becoming dilated and pouch-like, and by means of the confluence of contiguous dilatations, appear as widely dilated spaces communicating freely with each other.

In *hæmato-chyluria* the parasites probably have their seat in the thoracic duct or in one of its affluents, or in the tissues surrounding the abdominal aorta. Into this is discharged, not only the lacteal vessels of the intestine, but, amongst others, the lymph vessels of the urinary apparatus. If the parasites cause an obstruction in the places mentioned, an engorgement is set up in all these vessels, and the lymph which seeks to attain the blood by collateral tracts has to take a retrograde current in the dilated vessels. The degree of engorgement depends on the elasticity of the collateral vessels. If the engorgement is great the stretched vessels may at last burst. If this occurs in any spot in the urinary passage the chylous contents become mixed with the urine and chyluria ensues. In another case, to be mentioned below, Havelburg was able to confirm with certainty that the admixture of chyle with urine took place in the bladder. When the lymph passages burst, the blood vessels may become torn, also causing hæmaturia, particularly at the commencement of the attacks.[1] Moreover, it is possible that the veins also participate in the dilatations of the lymph varices, so that when the varix bursts there occurs an admixture of blood with the urine. As the engorged contents of the lymphatic and lacteal vessels find an outlet, partly in this manner, and partly by the collateral channels, the engorgement gradually decreases, the dilatation of the vessels is less, and in consequence the torn vessels are finally closed. The abnormal discharges then cease. When, however, the collateral passage cannot battle with the quantity of lymph, engorgement with its consequences is set up anew and the vessels at last burst. The repetition of this process brings about the intermittent characteristics of hæmato-chyluria, and it is for this reason that embryos are found in the blood of patients even during the quiescent intervals.

[1] Manson does not attribute the sanguineous admixture of the urine to the blood vessels being torn, but to the circumstance that the lymph so long retained in the varicose lymph passages transforms white blood corpuscles into red.

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The seat of filaria Bancrofti in hæmato-chyluria has not yet been established by *post-mortem* examination. To my knowledge there are only reports of four autopsies in literature. In neither of these cases, however, was the parasite found, either because it had already died and disappeared, or because the autopsies were not sufficiently thorough. The lymphatic vessels, however, presented the changes described above.

Ponfick's case, which is the earliest account we have of a *post-mortem* examination of a case of filarial disease, related to a patient who had acquired chyluria in Brazil eighteen years previously. At the autopsy all the lymphatic vessels of the abdomen and the trunk of the thoracic duct itself, were found to be dilated to the thickness of a finger ; no filariæ, however, were found. They had not been sought for during life.

Havelburg, in Santos (Brazil), conducted an autopsy on a woman who had suffered from chyluria and died from exhaustion and diarrhœa (chylous). He found in the left side of the abdominal cavity a large pouch with purely chylous contents, which was divided into many compartments and possessed numerous dilatations. Many nodules varying in size from a filbert to that of a walnut could be felt : these were the swollen dirty-red looking lymphatic glands, from the incised surface of which a thick white fluid mixed with blood could be expressed. Thick white cords extended over the mesentery as far as the small intestine.

Havelburg, even during the patient's life-time, was able to confirm the fact that the admixture of chyle with the urine had taken place in the bladder. The patient had, in fact, an unusually wide urethra, so that the bladder was easily accessible to digital examination. He therefore was able to pass a catheter into the ureter : the urine evacuated by this means exhibited quite a normal appearance.

In a case of Mackenzie's observed in London, the patient, who was a European, born in India and 25 years of age, died ten months after the appearance of the chyluria. About eighty days before his decease, a rigor took place, followed by the development of an abscess in the region of the left sterno-clavicular articulation ; double pleurisy then set in and a second abscess developed in the left acromial region, after which the filariæ in the blood had disappeared. At the autopsy right-sided empyema, left-sided pleurisy and pulmonary œdema, cystitis and commencing suppurative nephritis were revealed. The thoracic duct was obliterated $7\frac{3}{4}$ cm. above the aortic orifice in the diaphragm and appeared as a hard thick mass ; it was only $10\frac{1}{2}$ cm. higher that the duct could again be isolated, from whence it proceeded surrounded by a mass of lymphatic tissue to its ending in the angle between the left subclavian and internal jugular vein. Below the spot where the obstruction occurred, the thoracic duct and the receptaculum chyli were sinuously dilated and the dilatation proceeded to the lumbar, renal and iliac lymphatic vessels, which formed a close mass extending from the bifurcation of the aorta to the aortic orifice in the diaphragm, and filled the entire space between the two kidneys. No parasites at all were found in the coagulum contained in the thoracic duct nor in the dilatations of the renal lymphatic vessels of the left side.

Manson publishes a fourth case observed and examined by Curnow in Greenwich Hospital. It was the case of a sailor, aged 32, who was born in Burmah, of English parents. The patient died from miliary tuberculosis and right-sided serous pleurisy ; he suffered temporarily from chyluria with filariæ and two days before his death he also exhibited filariæ in the blood. The thoracic duct was much dilated in the thorax and was lost below the aortic orifice in the diaphragm in a large hard tumour situated in front of the vertebral column ; the tumour extended to the right iliac fossa and on the left side as far as the ureter ; $5\frac{1}{4}$ cm. below the left subclavian vein the passage was closed and the thoracic duct was lost in a tumour of similar construction to the lower one, but smaller, so that its anastomosis could not be found. The dilated passage was filled with a large clot. Both tumours were hard, tense, somewhat fibrous, of a greyish colour, and exhibited dilated lymphatic vessels on the incised surfaces. No burst or dilated vessels could be discovered in the urinary apparatus.

In *elephantiasis* of the legs and of the scrotum, the parent worms in most cases are probably situated in the lymphatic vessels near the groin glands. The inguinal glands become choked and finally so crammed by the products of the worms that the lymph is entirely unable to pass through. According to Manson the engorgement is principally occasioned by the eggs that have prematurely escaped from the body of the female parent and which are far thicker than the embryos. This obstruction to the onward passage of embryos explains why in elephantiasis frequently no filariæ are found in the blood. An engorgement of lymph and

dilatation of the lymphatic vessels at first takes place in the legs and scrotum, and frequently repeated inflammatory attacks gradually cause hypertrophy of the connective tissue. The hypertrophy affects in particular the skin, the intra-muscular cellular tissue, the aponeuroses, and the sheaths of the nerves and vessels. In recent cases, especially, small-celled infiltrations are embedded on many spots of the newly formed connective tissue. The muscles, in consequence of the pressure, may become atrophied or may be the seat of fatty degeneration. The blood vessels as well as the lymph vessels are found to be dilated, their walls thickened and the capillaries increased in numbers. The bones may be thickened and covered with osteophytic out-growths, or in rare cases may be atrophied. Sometimes circumscribed abscesses with caseous contents resembling those of tubercular changes may be seen in the bones. The epidermis is much thickened in some parts and in others almost unchanged. The papillæ are sometimes atrophied, sometimes enlarged, the sweat glands atrophied or their excretory ducts lengthened and the glandular elements degenerated, and similar changes occur in the hair follicles. Manson believes that circulating lymph is necessary for the life of filaria Bancrofti, and that therefore in elephantiasis, in consequence of the absence of collateral tracts, the stasis becomes complete or nearly complete and the parent worm dies.

It may be taken for granted that in those cases of *lymph scrotum* and *varicose groin glands* in which the contents of the dilated vessels are of a chylous nature the adult worms have their seat in the thoracic duct, and that these affections are but a part of the lymph-varices of the abdomen and pelvis. If, on the other hand, the fluid is not milky but clear, the seat of the adult parasite may be sought in the groin glands or their periphery, which in consequence of the obstruction set up by the ova, embryos or even the parent worms themselves, are impassable. In such cases the parasites will not be found in the blood. In lymph scrotum, as in hæmato-chyluria, a rupture of the dilated superficial lymph vessels of the cutis takes place.

Young, of Charing Cross Hospital, found the following pathological-anatomical conditions at the autopsy of a young sailor from Jamaica, aged 21 years, who for seven years had suffered from *lymph scrotum* and *varicose groin glands*, and finally committed suicide (hydrocyanic acid) :—The principal organs were normal. The spermatic cords on both sides were surrounded and permeated by a great mass of stretched, tortuous, and irregularly varicose lymphatic vessels. The inguinal canals, owing to the dilated lymphatics, were so large that three fingers could easily pass along them. The femoral and superficial inguinal glands were enlarged in some instances to the size of a small chestnut ; some were varicose. In front of the lumbar vertebræ there was a great mass of similar lymphatic tissue, which was 1 foot in length, 9 inches in breadth, and 3 inches in depth. The varicose lymphatic vessels exhibited a peculiar purple colour, and somewhat resembled in appearance the intestines of the rabbit. A few vessels were as large as the abdominal aorta, and through their thin transparent walls the faint brownish opaque contents—lymph or chyle—could be plainly seen. The kidneys were entirely covered and hidden by the mass of varicose lymphatics. Another group of varicose lymphatics, beginning in the pelvis, between the bladder and rectum, were connected with the dilated lymphatics coming from the scrotum and formed the chief retro-peritoneal mass. The receptaculum chyli could not be distinguished. The lacteal vessels were not dilated, the bowel and intestine were relatively empty. In the thorax, the dilated thoracic duct lay on the vertebral column to the left of the median line, its course was very tortuous, and here and there it was as thick as a man's forefinger, in other places less thick than in the normal. It was not possible to pass a probe from the interior of the left subclavian vein into the mouth of the duct, as the valves closed well, but on opening the thoracic duct a No. 3 (English) catheter could be pushed without difficulty through the valves. Unfortunately at the autopsy it was not possible to avoid incising the dilated lymphatics once or twice, when the chyle flowed quickly into te abdominal cavity. Out of one

cut made into a lymphatic vessel of the right groin, a small bundle fell; it had the appearance of a small ball of very fine catgut, and it consisted of a portion of the bodies of three female filariæ. On examining the lymphatic vessels of the right vas deferens, six females were found coiled up in a sinus or behind a valve; on the left side there were six females and one male. No parasites were found in the retro-peritoneal mass, but it was not possible to examine this minutely, in consequence of its condition. During life, a lymphatic varix containing one female, had been excised from the patient's right forearm.

In *orchitis* and *chylocele* the adult worms probably are situated in the thoracic duct; the varicosities extend from the lymphatic vessels of the abdomen to those of the vas deferens, and through the bursting of the latter a chylous effusion takes place into the tunica vaginalis.

It would be imagined that by means of the dilated lacteal vessels bursting into the peritoneal cavity *chylous ascites* would be set up; but as already mentioned, no observations have hitherto been made of such an occurrence.

The rupture of the dilated lacteal vessels into the intestine explains the appearance of *sanguineous* and *chylous diarrhœa*.

It will therefore be noted that the seemingly heterogeneous diseases comprehended under the collective name of *filaria disease*, are essentially attributable to the same ætiological factor.

Should the parasites take up their abode in a place where they engender no obstruction to the flow of lymph, as, for instance, in the wide receptaculum chyli, it is quite possible that filaria embryos may be met with in the blood of seemingly perfectly healthy persons.

It is possible that other causes may originate the same disorders as filaria Bancrofti. Sporadic cases of chyluria, elephantiasis and lymphor-rhagia are occasionally observed in Europe where the filaria is not endemic. Some of the lymphangiomata decidedly belong to this category. It is not, however, advisable to cast aside the possibility of a parasitic origin in all cases from the mere fact that repeated examinations have failed to reveal filarial embryos in the blood, urine, &c. Should the person affected be living in countries where filarial disease occurs endemically, or should he have ever previously lived in such countries, filarial infec-tion must be considered to be a possible cause. If during the further course of the disease the parent worms perish no embryos or ova will be found, for even if formerly present they disappear after some time by becoming dissolved or by being carried off by the urine or some other normal or abnormal secretion or excretion; but the local disorder which they have caused persists. Embryos also cannot be found if the adult worm of one sex only is present, as no propagation can take place.

Ever since the filaria sanguinis hominis was first observed we have been acquainted with the fact that—probably dependent on the periodical deposit of the embryos by the parent worm—at one time the embryos will be found in the blood of a patient, and at other times in the same person they will be absent.

Moreover, as we have already seen there are cases in which the embryos do not reach the blood at all, although they are present in the fluid secreted in lymph scrotum, the lymph of varicose glands, &c. This is primarily the case when the dwelling place of the filaria is immediately adjacent to lymphatic glands which are crammed so full of embryos and ova that the passage of lymph through them is completely suspended.

In 1879 Manson made the following exceedingly interesting discovery. Even when the lymph passages are free no *embryos* or only very few are to be found in the blood during the day, in the *night*, however, they swarm

in it.   A few first appear in the evenings, they attain their maximum at midnight, their number then again decreases and they disappear in the early morning hours.   This observation, which Manson first made on patients with elephantiasis and lymph scrotum, was very soon confirmed by many observers, myself amongst them, on patients suffering from hæmato-chyluria.   This discovery explains why so many examinations of blood which were naturally undertaken during the day had negative results. Night-time, preferably the hours between 11 p.m. and 2 a.m., should be chosen for making blood examinations.

  Hitherto no satisfactory solution as to the reason for this extraor-dinary phenomenon has been forthcoming.

The explanation which was first given by Manson himself is wholly teleological, and it takes for granted that the filaria adapts itself to the nocturnal habits of its inter-mediary host; in conformity with a certain *instinct* the embryos circulate in the blood at night because the mosquitoes swarm during this time, and the embryos must be taken up by them in order to develop further; during the day they rest in certain organs of the thorax and abdomen, probably clinging to the inner surface of the vessels by their heads.   In the above mentioned case of lymph scrotum and varicose groin glands (see above, p. 403), in which death occurred about 8.30 a.m.—thus at a time at which the embryos had retreated from the peripheral circulation—a few were found in the capillaries of the muscles and of the brain, as well as in the renal vessels; a con-siderable number were found in the myocardium; most, however, were found in the blood vessels of the lungs, while the liver, spleen, and bone marrow exhibited very few or no embryos.

Lancereaux, who conjectured that *light* exercised some influence, shut a patient up in a dark room for a whole day, but could find no filaria in his blood.

Myers believes that the embryos lead an ephemeral life in the blood, that they are drawn into it in the night in consequence of its containing more oxygen at that time, and die off in the morning in consequence of the relatively small quantity of oxygen then present in the blood.   He states that in the mornings he has always found the embryos sluggish, stretched-out, dying, or even dead, whereas in the evenings they move about more briskly; during the day, however, he was never able to find the remains of dead embryos.   I have not been able to confirm Myers' observation.

The most plausible opinion that the nightly circulation of the filaria embryos in the blood is caused by the *periodical*, daily repeated *deposit* of them by the parent worm is contradicted by the fact that chylous urine as well as the lymph oozing from a lymph scrotum contains embryos at all times of the day, as Manson found.

The following facts clearly prove that "*filarial periodicity*" is not caused by the manner of life of the parent worm of the embryos, but that the phenomenon is much more probably attributable to the *motor and digestive functions of their host* :—

(1) I treated a young Japanese suffering for two months from hæmato-chyluria with picric-nitrate of potash for three weeks.   During this treatment the urine improved in appearance, and the blood disappeared from it; the number of filarial embryos in the urine as well as in the blood decreased; the embryos which previously had exhibited lively movements were now found by me to be motionless, dead, or only endowed with a trace of life.   Even these motionless dead embryos only appeared in the blood at night, while, as previously, it contained none during the day.   Four months after having discontinued the drug this peculiar phenomenon was still to be observed.

(2) A young East Indian soldier, suffering from hæmato-chyluria, came under Mackenzie's treatment in London.   This observer, after having confirmed the presence of the filarial embryos in the blood during the night, entirely reversed his patient's manner of life by letting him go about at night and sleep by day.   The filariæ then disappeared from the blood in the night and could only be discovered there during the day.   Mackenzie's observation was confirmed by Manson, who likewise found that when patients, for several days, are allowed only to sleep for a short time and at short intervals, the periodicity vanished, and the filariæ are exhibited in the blood at all times.   Change of meal-times had, however, no influence on the phenomenon.

The explanation given by me is grounded on the above observations.   The passage of the lymph or chyle, accompanied by embryos from the vessels occupied by the parasites into the blood is naturally dependent on the degree of obstruction which they occasion, and on the capacity of the collateral tracts that have been formed.   This obstacle will be still more pronounced if there is an acceleration of the flow of lymph through them, as is known to be the case in movements of the extremities.   During the absolute rest of sleep favourable conditions are afforded to the embryos to pass along and gain the circulation.   Moreover, the horizontal position assumed and the deep breaths

drawn during sleep accelerate the flow of lymph into the blood. When the lymphatic region attacked by the disease is completely cut off from the lymph stream, as occurs frequently in elephantiasis of one leg, no embryos can reach the blood from thence, even during the recumbent position.

According to v. Linstow, the nocturnal appearance of the embryos in the blood is intimately connected with sleep, and depends on the fact that the peripheral cutaneous vessels are somewhat dilated during sleep, but are contracted during the waking condition. This contracted capillary system of the skin cannot be passed by the filariæ; they therefore rest by day in the larger branches deep in the cutis.

Lately Manson has come to the conclusion that the periodicity is attributable to some physiological product of metabolism that forms during the waking hours and which during the day drives the embryos from the surface of the body, or draws them to certain internal organs.

Thorpe could not confirm periodicity in the Friendly Islands. In ninety-six cases of natives the embryos were seen in nearly equal numbers day and night. Thorpe attributes this to the custom of the natives to sleep at irregular times, transforming night into day and *vice versâ*.

The embryos that have invaded the blood are most probably removed from the body by means of the various secretions, so that by day the blood again appears to be free from them. Filarial embryos have even been found in the tears of filaria patients.

Manson designates the filaria Bancrofti, in consequence of the nocturnal appearance of its embryos in the blood, as *filaria nocturna* and differentiates *filaria diurna* and *filaria perstans* from it.

The embryos of *filaria diurna* (see fig. 42 *b*, p. 398) exhibit a reversed periodicity; they commence to appear in the blood at about 9 or 10 a.m., they increase in numbers up to 1 or 2 p.m., then again decrease and disappear at 9 or 10 p.m. They do not differ from the embryos of filaria nocturna in their size or structure; the latter, however, in thicker layers of blood exhibit more graceful curves than the former.

Manson found the filaria diurna in the blood of three healthy negroes from the West Coast of Africa (where filaria Bancrofti is also endemic), and he is of opinion that the *filaria loa* is the parent worm, and that *Chrysops dimidiatus* (van der Wulp), a species of fly that sucks by day, and which is common in Old Calabar, is the intermediate host.

As the differences found by Manson between the embryos of filaria nocturna and filaria diurna are quite minor, as we have seen, and as the former exhibits deviations of its normal periodicity dependent on the condition and state of its host, I should be loath to establish the identity of either. If Manson's opinion were correct most of the observers who found filariæ in the blood of sufferers from hæmato-chyluria, elephantiasis, &c., previous to Manson's discovery of "filarial periodicity," could not have found filaria Bancrofti, for it must be conceded that examinations are usually undertaken in the day time.

The embryos of *filaria perstans* (see fig. 42 *e*, p. 398), which are found in the blood by day as well as by night, are smaller than filaria nocturna. Manson found that dead, or nearly dead, embryos measured 0·209 mm. in length, and 0·004 in breadth. The posterior two-thirds of the body are thinner than the anterior third, and they have a stumpy or rounded-off caudal end and no sheath. The head (see fig. 43 *a* and *b*), examined by an immersion lens, is seen to be different from that of filaria nocturna (see fig. 43 *c* and *d*). The head of the latter possesses a broad, round tongue, carrying an exceedingly delicate process, and surrounded by six lips. The tongue can only be seen when the lips are drawn back, and it disappears when they are closed, and overlap each other. From the head of filaria perstans a fine needle-like process is seen, which, like the tongue of a serpent, darts forward from time to time, and then is withdrawn from sight. Manson considers that this is a boring apparatus. He has not minutely examined the head of the filaria diurna. Moreover, filaria perstans lacks a peculiar formation which Manson has observed in the filaria nocturna as well as in the filaria diurna; examined by an immersion lens, at 0·058 behind the head, a triangular V-shaped light spot is observed, the point of which is directed to the periphery of the filaria, and which conveys the impression of a cavity; it is regarded by Manson as the rudiment of a vagina.

The movements also of filaria perstans are different from those of the other two filariæ; whereas the latter, in spite of their lively mobility, do not stir from one place, the filaria perstans, at least at times, shows a worm-like and serpentine progression, and possesses also a higher capacity to elongate and shorten its body whilst moving

forward. Manson, however, has also observed locomotion in embryos of filaria nocturna that had cast off their armature, a phenomenon that can be seen if the blood preparations are left in the cold over night.

The parent worm of filaria perstans has hitherto been found three times. Twice by Daniels in British Guiana, and once by O'Neil in Charing Cross Hospital, in a negro with sleeping sickness. The parasites were situated in the fat of the mesentery in the vicinity of the pancreas, in the sub-pericardial fat and in the connective tissue behind the abdominal aorta. The filaria perstans is smaller and thinner than the filaria Bancrofti (the female 70 to 80 mm. in length and 0.12 mm. in breadth ; the male 45 mm. in length and 0·06 mm. in breadth), but otherwise bears some resemblance to it. It is minutely described by Daniels in the *British Medical Journal* of April 16, 1898, p. 1011.

The *West Coast of Africa* with the contiguous hinterland, and *British Guiana*, are known as the region of distribution of filaria perstans. Manson is also of opinion that the filariæ observed by Firket, in the negroes of the Congo, are filaria perstans.

As to their pathological significance, Manson connects them with the skin disease known on the West Coast of Africa as *kro-kro* (*craw-craw*), and also with *sleeping sickness of the negroes*. The negroes, however, in whose blood he found these parasites, were quite healthy.
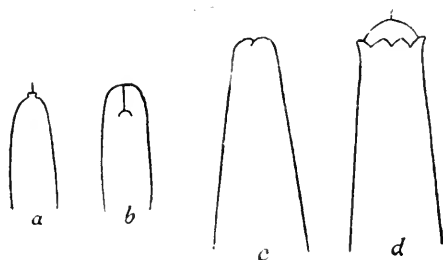
Fig. 43.—Head end of *filaria perstans*, (*a*, *b*), and of *filaria nocturna* (*c*, *d*), after Manson.

Manson discovered still another species of filaria in blood preparations, from St. Vincent (West Indies), and called it *filaria Demarquayi* (see fig. 42 *c*, p. 398). The embryos are less than half the size of filaria nocturna, have no sheath, and are found in the blood by day as well as by night. Galgey also found them in St. Lucia (West Indies). They are probably identical with one (the sharp-tailed) of the two sorts discovered in British Guiana, by Ozzard and Daniels, and which have been designated *filaria Ozzardi* by Manson, while the other (the stump-tailed) has proved itself identical with filaria perstans.

The pathological significance of filaria Demarquayi is not yet known. Their parent worm was probably first found in British Guiana by Daniels. At the autopsy of a native Indian, whose blood had exhibited sharp-tailed as well as stump-tailed embryos, Daniels, besides finding several filaria perstans in the sub-peritoneal connective tissue, came across a female and the fragment of a male of another kind of filaria, which was distinguished from filaria perstans by being of about similar length but nearly double its thickness (the female was 81 mm. long, and 0·21 thick ; the male 0·2 mm. thick). Daniels proposes that the designation *filaria Ozzardi* be retained for these. He describes them minutely in the *British Medical Journal* of June 17, 1899, p. 1459.

Filaria Kilimaræ is the name given by Kolb to a white filamentous worm, related to filaria medinensis, and of which only female specimens have hitherto been observed ; it is 10—20 cm. in length, and 0·5—1·0 mm. in breadth. Kolb found it in British East Africa, in the stools and vomit of negroes, in the cadaver, and between coils of intestine ; he also found it in fishes, in the hippopotamus, the zebra (in hepatic pus), the rhinoceros (in the peritoneal cavity, with sero-sanguineous fluid), in the Oxyx-beisa buck (in the liver), and in stagnant waters. He believes that the *Massai disease*, which occurs during the rainy season, and is manifested by abdominal pains, rigors, fever, general languor, loss of appetite, sometimes diarrhœa and vomiting, and a peevish frame of mind, and from which negroes sometimes die, is attributable to this kind of filaria. Kolb believes that many of the unexplained fevers in Europeans are due to this cause.

DIAGNOSIS.

The diagnosis of filarial disease as a rule offers no difficulties.

Hæmato-chyluria is easily distinguished from cystitis, pyelitis, abscesses which have burst into the urinary passages, hæmoglobinuria and ordinary hæmaturia, by the examination of the urine.

The microscope must be brought into requisition in countries where, as in Egypt, Mauritius, Madagascar, besides *filaria sanguinis hominis*, bilharzia hæmatobia is endemic. In the former embryos are found in the urine, in the latter ova. It is possible also that the same patient may shelter the two parasites.

Confusion of elephantiasis with leprosy which formerly obtained, and which was principally caused by the unfortunate choice of the same name for the two diseases, can easily be avoided by the consideration of the widely different symptoms.

Steatopyga, which occurs in Hottentot and negro women, and which consists in hypertrophy of the adipose tissue over the gluteal muscles, and which in pregnancy is apt to increase, similarly to the increase in the circumference of the breasts, could scarcely be confused with elephantiasis.[1]

Lymph scrotum also is easily distinguishable from other diseases, especially eczema.

Under certain circumstances varicose groin glands have been mistaken for hernia, even by such surgeons as Trelat and Nelaton (Manson). In the differential diagnosis it should be borne in mind that varicose groin glands are not influenced by coughing, that a dull percussion sound is elicited, that on taxis it disappears slowly, not suddenly like hernia, and without gurgling. Magalhães recommends for the differentiation of hernia from varicose groin glands, that the patients should lie on their back with a pillow under the buttocks; if the disease is varicose groin glands it will be observed that the swelling gradually grows smaller and finally vanishes altogether. If the patient then stands up and one's hand is placed on the region of the swelling it can be felt to slowly re-appear.

Filarial orchitis and hydrocele or chylocele are distinguished from other forms of these diseases by the presence of the embryos.

In other particulars the diagnosis of filarial disease is confirmed by what has been mentioned above.

PROGNOSIS.

The prognosis of filarial disease is *not unfavourable*. It may persist for years without essentially injuring the general health. Cures very rarely occur. Mazaé Azéma states that varicose groin glands may disappear after years, but the patients never recover their former health.

PROPHYLAXIS.

If Manson's opinion, that filarial disease is due to the drinking of water polluted by mosquitoes containing the larvæ of filariæ, is correct, the way to ward off the disease is evidently to boil and filter all doubtful waters before using them.

[1] Däubler, *Die Grundlage der Tropenhygiene*, Munich, 1895, p. 80.

The general introduction of *mosquito nets* is a further desideratum in countries where this disease is endemic, this measure making it impossible for mosquitoes to suck embryos from the blood of diseased persons.

TREATMENT.

Several *parasiticide drugs* have been recommended for the cure of filarial disease : benzoic acid, benzoate of soda, boric acid, thymol, have all been tried, but the results achieved have not been encouraging. Even if the parasites are killed by such drugs—as occurred in my own case by picric-nitrate of potash—nothing is gained, for the disorders originated by the parasites still persist. Manson is even of opinion that the well-being of the parasite is an advantage to its host ; for as already observed, the formation of abscesses is sometimes caused by the death of the parasite.

Flint, on the grounds of an ostensibly cured case of chyluria, has lately recommended *methylene blue* (0·12 every four hours). Zellweger found that methylene blue yielded good results in five cases of lymph scrotum and chyluria. Henry found methylene blue absolutely inefficacious in one case of chyluria, for though the filarial embryos were stained blue, their viability did not seem to be affected.

Concerning the treatment applicable in the diverse conditions set up by filarial disease, remedial measures vary with the several forms the disease presents. In *hæmato-chyluria* rest in bed has a good effect. By this means the pressure in the chyle-vessels is diminished, so that the closing of the fistulous communication between them and the urinary passages is facilitated. Rest in bed also renders it possible to diminish the supply of food, by which measure the contents of the lacteals, &c., is likewise diminished. De Arze recommends a diet consisting of albumen and farinaceous food, *i.e.*, a diet poor in fat and water. Sonsino recommends santal oil for chyluria, and Moncorvo ichthyol (0·5—1·5 per diem in the form of pills).

The treatment of *lymphangitis* necessitates rest, an elevated position of the part affected, the use of ice locally, and the inunction of mercurial ointment.

In *elephantiasis of the legs*, rest, an elevated position of the limbs, massage, methodical compression by means of roller bandages of linen, flannel, or india-rubber, applied from the sole of the foot to above the border of the thickened part, are indicated. In addition, the application of tincture of iodine, iodide of glycerine, iodine or mercurial ointments is useful. Hot water baths and steam baths are efficacious in rendering the skin softer and more pliable. Moncorvo and Da Silva Aranjo have for some time treated cases of elephantiasis with the constant current with favourable results, and have assisted the liquefaction of the masses of tissue by periodical application of the induction coil. These observers also made use of electrolysis, but have given no details as to their procedure. Manson recommends the excision of strips of thickened skin in the longitudinal axis of the legs. The ligature and compression of the afferent arteries are methods that have also been tried in elephantiasis, but with dissimilar results. Ligature of arteries should be entirely dispensed with on account of its danger. Of twenty-three cases of ligature of the femoral described by Wernher, eight (thus more than 33 per cent.) ended fatally, three from pyæmia and erysipelas, two from gangrene of the foot, and three from profuse hæmorrhage (v. Hebra).

In the acute attacks Manson recommends puncturing with a sharp lancet under antiseptic precautions.

Elephantiasis of the scrotum may be removed by operation. Manson recommends that it should be preceded by elevation of the scrotum, so that the tumour becomes softer through being partly emptied of lymph ; in malarial countries also, the administration of quinine is advisable for three or four days (0·3 three times a day) prior to the operation. The operation itself, according to Manson and Müller, is conducted in the following manner :—

After having suitably marked out the place where the tumour is to be amputated by shallow incisions in the skin, and traced out the flaps, an elastic ligature is applied round the neck of the tumour and fastened round the waist. A long incision, reaching from the external abdominal ring, is carried downwards and parallel to the spermatic cord on one side. By this incision the cord and testicle are exposed when they are to be separated from their environment by enucleation, mostly by the fingers. The gubernaculum testis is finally divided, and the cord and testicle, wrapped in antiseptic gauze or lint, are thrown up on the abdominal wall. The process is repeated on the other side. The penis is to be exposed by an excision along the dorsum reaching from near the root of the organ to the urinary orifice in the scrotum. The prepuce is now divided around the glans penis and the whole organ shelled out from its surroundings. If sufficient healthy tissue is obtainable whereby to form flaps, they are to be reflected, the vertical incision over the cords and the penis are united by horizontal incision, and then, while the flaps with the penis and testicles, are held aside, the remainder of the neck of the tumour is severed, taking care not to wound the perineal fascia. The mouths of any blood vessels that are visible are ligatured, the elastic cord is then loosened, and the hæmorrhage is arrested. If hydroceles are present these are now incised and all superfluous tunica vaginalis removed. The testicles are then covered by the lateral flaps, which are sutured ; the upper third of the lateral flaps are united with the edge of the horizontal incisions ; when a T-shaped wound results with the penis protruding between the horizontal and vertical incision. An antiseptic dressing is then applied. As soon as the penile surfaces commence to granulate they should be covered by a skin grafting. Great care must be taken that the penis does not become adherent to other parts of the wound.

Ali-Bey recommends that a flap be taken from the cutaneous structure over the front of the symphysis pubis above the penis and brought down so as to cover the penis as much as possible, when it is sutured to the penile tissues, after the perinæum is covered by the lateral flaps, the upper and lateral flaps are to be stitched together.

Maitland, after the mass of the scrotum is removed, obtains flaps by undermining the cutaneous structures of the thighs contiguous to the perineal wound. The edges of these lateral flaps are sewn together along the centre of the perineum, so that pouches are formed for the testicles. The upper edges of the lateral flaps are then sewn to the root of the penis, and when granulations appear skin grafting is resorted to, in order to obtain a satisfactory covering to the penis.

Amputation of the scrotum gives excellent results ; Manson (Amory), only lost five patients out of a total of 120 cases he operated on. Turner (Samoa Islands) lost two patients out of a total of 132 cases operated on. Relapses, however, are frequent, as usually all the diseased parts are not removed, and above all, because the cause of the evil cannot be done away with.

Elephantoid tumours of the female genitals frequently require to be removed on account of their size. The tumour, which is frequently pedunculated after being rendered bloodless, is simply removed, when the edges of the wound are united.

Lymph scrotum may require to be removed when the part is the seat of frequent attacks of lymphangitis, when the nutrition of the patient suffers through the repeated and continued lymphorrhagia, or when the patient is prevented from following his occupation on account of the disorder. Operation is also indicated when lymph scrotum is transformed into elephantiasis of the scrotum. The operation is conducted in the following manner :—

The mass of the scrotum is pulled down with the left hand, whilst an assistant presses the testicles up towards the inguinal canal. Two lateral flaps are formed,

PLATE V.

Fig. 39.
ELEPHANTIASIS OF THE SCROTUM in a Chinaman.

the superfluous portion of the scrotum is removed as close to the testicles as possible and the flaps are sewn together.

Manson, however, frequently observed that this operation was followed by chyluria, or elephantiasis of one leg.

In the case of *varicose groin glands* it is advisable to wear a suitable pressure bandage. Should the gland affection cause serious disorders, or induce frequent acute attacks, the removal of the enlarged glands and the dilated lymphatic vessels is indicated.

A double ligature must previously be applied round the lymph vessels, and if, in spite of this, lymphorrhœa should set in, the part must be plugged for several days.

Hydroceles and chyloceles seldom attain a size necessitating tapping. Mastin advises that the tunica vaginalis be cut into and the open lymph vessel excised or tied.

Abscesses forming in filarial disease should be treated like ordinary abscesses.

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VI.

ANCHYLOSTOMIASIS.

SYNONYMS.

Ankylostomasie, Ankylostomo-anæmia, die Ankylostomen Krankheit, Dochmiosis.

HISTORY.

Anchylostomum duodenale was discovered in Milan by Dubini in 1838. In 1846 it was found by Pruner, and a few years later Bilharz and Griesinger discovered the parasite in Egypt, and Griesinger recognised it as the cause of *Egyptian chlorosis.* Wucherer, in 1866, found the worm in Brazil and attributes the *tropical chlorosis,* so prevalent in those parts, to its influence. In 1877 and 1878 in Italy, Grassi, C. and E. Parona, and others, called attention to the occurrence of the parasite amongst brick-makers, and this observation was later on confirmed in Germany. The epidemic appearance of anchylostomiasis amongst labourers and engineers engaged in the construction of the St. Gothard's tunnel, excited great attention during the following year, the nature of the disease having been first recognised by Perroncito and Concato. After the completion of the tunnel the dispersion of the labourers caused the spread of the disease over a wide district of Italy. This epidemic called attention to *miner's anæmia* and *mine cachexia.* Perroncito was the first to point out that these ailments were at least partly caused by the anchylostomum duodenale.

Though our knowledge of the parasite is only of recent date the disease it causes has long been known. Joachim[1] believes that a disease described in an Ebers papyrus, and which is supposed to date back to 1550 B.C. at the latest, refers to anchylostomiasis. The first news of the disease came from Brazil to England in the seventeenth century, Piso in 1648 reporting a disease—*Oppilatio*—which is undoubtedly a Latin conversion of Oppilaçao, the present popular term for the disease there.

The following are more designations under which the disease has been described : *Egyptian chlorosis, anæmia of Ceylon, Tropical chlorosis, anémie des pays chauds, Hypoaemia intertropicalis, Geophagia, dirt-eating disease, Allotriophagia, mal d'estomac, mal de cœur, cachexia aqueuse, cachexie africaine, Amarellão* (jaundice), Cançação (fatigue), &c.

GEOGRAPHICAL DISTRIBUTION

Though anchylostomum duodenale does occur in temperate zones, it is *principally warm countries* in which it is endemic, and generally distributed amongst the population.

In Africa the geographical regions of distribution of the parasite are Egypt, Abyssinia, Tunis, Algiers, Madeira, the West Coast of Senegal as far as the Congo, Cape Colony (Kimberley Mines and De Beers Mines), Natal, Orange River Colony (Bloemfontein), German East Africa (district of the Kilima Njaro), Zanzibar, the Comores, Madagascar and Mauritius.

[1] Die Heilkunde der alten Ægypter nach dem Papyrus Ebers. *Transactions of the X. Intern. Med. Congr. Berlin,* 1890, vol. v., part 16, p. 37.

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In Asia the parasite is found in Travancore, Bengal, Assam, Madras, Ceylon, the Malay Peninsula and Archipelago, Luzon (Manila) and Japan.

In America the disease is observed in a few *southern states* of the United States (Louisiana, Alabama, Georgia, South Carolina and Florida), Mexico (Guanajuato), Central America (Guatemala, San Salvador, Costa Rica), the Antilles, Columbia, Venezuela, Guiana, Brazil, Argentina (Buenos Ayres), Peru and Bolivia. The disease occurs also in Australia (Queensland), New Guinea and the Fiji and Sandwich Islands.

In Europe the anchylostomum has been observed in Italy, Sicily, Sardinia, amongst the *labourers* in the St. Gothard's tunnel ; amongst the *miners* in Carniola (Franzdorf), Styria (Leoben, Trifail, Kœflach), Hungary (Kremnitz, Shemnitz where the disease may probably be traced back to 1777, Brennberg near Oedenberg, Fünfkirchen, Resicza, Anima in the Banat), Rhineland and Westphalia (Aix-la-Chapelle, Bardenburg), Essen, Bochum, Dortmund, Castrop, Mengede, in Belgium (Liege, Limburg, Mons), in France (Anzin, Valenciennes, Commentry, Lyons, St. Etienne) ; and amongst *brickmakers* in Germany (Cologne, Bonn, Wurzburg, Berlin, and near Kösen).[1] The cases met with in Germany were those of Italian or Belgian labourers who work in summer in the German brickfields, and who work in winter in the Belgian mines.

In a few countries anchylostomum is distributed in so remarkable a manner, that a large percentage of the population is affected by the parasite. In Milan, Dubini found it in 20 per cent. of the autopsies. In Egypt, during Griesinger's time, about one quarter of the population of Egypt was suffering from anchylostomiasis. Tonsino, in 1877, found the worm in sixteen autopsies, and in Cairo in nineteen. In Upper Egypt, according to Sandwith, 3·3 per cent., in Lower Egypt 6·2 per cent., and in the province of Menoufieh even 13·9 per cent. of the recruits are rejected in consequence of anæmia. In Madras, according to Williams, of fifty cadavers examined, twenty-six, *i.e.*, 52 per cent. exhibited anchylostoma, and in Budaon (north-western provinces), according to Close, of 81 cadavers 44, *i.e.*, 54 per cent., exhibited the same condition. In Java (Batavia) I found this intestinal parasite in 88·2 per cent. of autopsies (15 times in 17 cases), in Japan (Kioto) in 13·5 per cent. (5 times in 37 cases). In Guatemala Prowe found anchylostoma 46 times in 83 cadavers, *i.e.*, in 55 per cent.

NATURAL HISTORY OF ANCHYLOSTOMUM DUODENALE.

The *anchylostomum*[2] *duodenale*, or *dochmius duodenalis* (Leuckart)[3] belongs to the order of the *nematodes* and to the family of the *strongylides*, and is a cylindrical, fairly thick worm. The head, which is bent towards the dorsal surface, is conically pointed and provided with a protruding oral capsule. At its upper ventral edge there are four strong claw-like hooks ; two smaller ones are placed at the opposite dorsal edge and two more pointed processes lie deeper within the oral capsule (see fig. 46

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[1] Bernheim's case observed in Soellingen, in the Grand Duchy of Baden was, with justice called into question by Huber (*Centralbl. für Bakt.*, 1898, Nos. 5 and 6, p. 207) ; it was more probably a case of oxyuris vermicularis.

[2] Derived from ἀγχύλος, *i.e.*, hook, and στόμα, *i.e.*, mouth, therefore hook-mouth.

[3] Other synonyms are : *Strongylus quadridentatus* v. Siebold, *Dochmius anchylostomum* Molin, *Sclerostoma duodenale* Cobbold, *Strongylus duodenalis* Schneider.
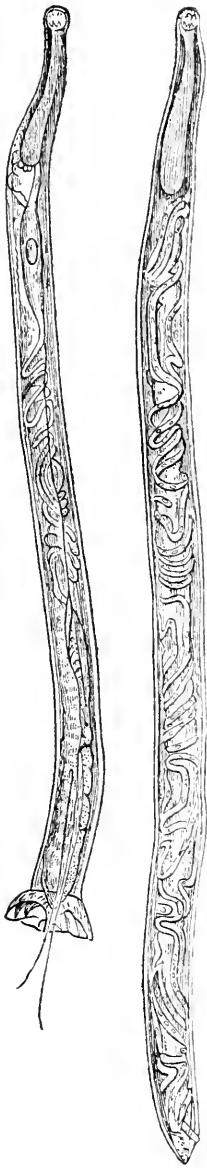
below).   The hinder end of the head capsule communicates with the very muscular pharynx, and to this is attached the large intestine which is often filled with more or less fresh blood, and thus gives the worm a reddish or brown colour; when the digestive canal is empty the worm has a whitish appearance.

The *male* (see fig. 44), which according to Leuckart is 6—8 or exceptionally 10 mm. in length, terminates in a bell-shaped bursa with a bottle-shaped penis and two long thin spicula.   The bursa is provided with eleven ribs, five on each side, and a dorsal rib, which at the distal end splits into two prongs each carrying three short conical processes.   Four out of the five lateral ribs are attached to one common trunk, while the fifth emerges from the root of the dorsal rib.   The male sexual apparatus is a simple long tortuous canal, consisting of the testicle and spermatic duct, the oval or fusiform seminal vesicle, and joined to this a long wide ejaculatory duct.

The female (see fig. 45), which according to Leuckart is 10 to 12 and more rarely even 18 mm. in length and about 1 mm. in breadth (the male is somewhat thinner), has a conically pointed caudal end.   The vulva lies behind the centre of the body, and a short tube leads from it into a double muscular vagina, to which an anterior and posterior uterus is joined, both of which lead to a tortuous long ovary.

FIG. 46.—*Oral capsule* of anchylostomum duodenale.   After Leuckart.

In copulation the male grasps the body of the female by means of the bursa, which is fixed by the introduction of the long spicula, at the entrance of the vulva.   Such little couples have the form of a γ (Sonsino); but it is very rarely that anchylostoma are discovered in this position.

When coupled together during copulation the worms resemble in outline the Greek letter γ.

The *ova* (see fig. 47) are on an average 60 μ in length and 40 μ in breadth, of an oval shape, and provided with a very thin, simply outlined shell which is divided from the greyish yolk by a zone of clear, transparent fluid.   They are as a rule deposited when segmented and are evacuated with the stools of the patient.   In fresh stools the yolk is found to be divided into two, four, or even eight globules; it is only very rarely that ova are found unsegmented.   If the stools are allowed to stand

FIG. 44.   FIG. 45.

FIG. 44. — *Anchylostomum duodenale; male.* After Perroncito.   Enlarged ten-fold.

FIG. 45. — *Anchylostomum duodenale; female.* After Perroncito. Enlarged ten-fold.

a little while the segmentation becomes complete, and the rhabditiform stage is attained.

The statements of authors as to the size of the ova vary considerably, as will be seen from the following table :—

Leuckart	..	..	..	..	..	44-50 μ long and 23-27 μ wide.
Meuche	..	..	..	..	..	70 ,, ,, ,, 40 ., ,,
Bugnion	..	..	..	..	..	60 ,, ,, ., 40 ,, ,,
Railliet	..	..	..	..	..	52-62 ,, ,, ,, 32-43 ,, ,,
Bizzozero	..	..	..	..	..	58-62 ,, ,, ,, 38-40 ,, ,,
Leichtenstern		..	..	..	..	56-63 ,, ,, ,, 36-40 ,, ,,
Blanchard	..	..	..	..	..	55-65 ,, ,, ,, 32-43 ,, ,,
Sonsino	..	..	..	..	..	50-69 ,, ,, ., 30-40 ,, ,,

According to Leichtenstern, if properly magnified with stronger lenses, it will be perceived that there is another very delicate outline within the contour of the shell and lying close to it.
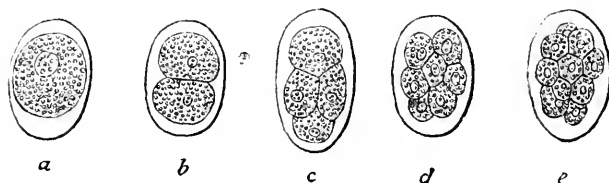
FIG. 47.—*Ova of anchylostoma* in various stages of segmentation. After Perroncito. Magnified 300 times.

The anchylostomum duodenale lives in the *upper part of the small intestine.* The jejunum and not the duodenum is the region of the intestine chiefly inhabited by the parasite according to Dubini. It has even been found in the ileum far beyond its middle, and even in the cæcum (Riou Kérangal) ; it is rarely found in the stomach. The worm is fastened between the folds of the mucous membrane by its head : the oral capsule, like a cupping glass, draws a piece of the mucous membrane into its cavity and fixes it with its teeth as with barbed hooks. The worm opens the blood vessels with the pointed processes at the base of the capsule and imbibes the blood. It probably only lives on the plasma without digesting the corpuscles, as these are mostly evacuated by the worms unchanged.

The anchylostomum is found in hundreds and thousands in the same intestine, the females generally preponderating in numbers. Bilharz states that the proportion of males to females is as 1 : 3, Lutz 2 : 3, Leichtenstern 10 : 22, van Emden 2 : 2·8. Bilharz's opinion is founded on observations made at autopsies, the other authors ground their statements on the number of ejected worms counted. Only in two cases did Leichtenstern find more males than females. Like Bilharz, I found one male to three females in the cadaver. Sandwith, however, in contradistinction to the observations of other authors, in 50 cases found 56 per cent. of males and 44 per cent. of females (*i.e.*, 10 : 8).

The anchylostomum, besides being found in man, has been discovered in the *gibbon* by Léon Levaillant, and in the *gorilla* by Leuckart.

As to the discovery of the worm in other animals, namely horses (v. Rathonyi) and dogs (Gray), there was probably confusion with other anchylostoma. Looss succeeded experimentally in transmitting the anchylostoma to young cats and dogs just weaned from their mother, but they never in these animals produced mature eggs, the parasites being previously ejected from the bowel.

Segmented ova of anchylostoma cannot develop into *embryos* and *larvæ* in the intestinal canal of man, as they lack oxygen there. The

development, however, occurs if the fæces containing ova is spread out and exposed to a temperature of 25—30°. Moist earth or a mixture of earth and fæces may be used for cultures. A temperature of 1° after an exposure of twenty-four to twenty-eight hours, kills the ova without exception (Looss). The fact that the anchylostomum requires a relatively high temperature for its development explains why this parasite, the principal breeding places of which is in hot countries, exists in temperate climates where its tropical requirements are present as in mines and tunnels.

According to Leichtenstern the most favourable medium for culture is the fæces, unchanged except for the admixture of some water to stir it into a thick pulp, and which is spread on a large glass plate; the eggs do not develop in thin liquid media. Immediately adjacent to the fæcal culture a·rim of water is placed into which the aquatic larvæ swarm, or a hole is made in the centre of the fæces, and this is filled with water. By filtering the water containing larvæ through blotting paper, the culture can be isolated, for the larvæ actively bore through the blotting paper, on the surface of which particles of fæces are left (Looss).

The embryo, according to Leichtenstern, develops in from one to a few days, and bursts through the end of the egg-shell sometimes head first, sometimes tail first. The embryo is from 200—250 μ in length and 15—17 μ in breadth, and exhibits lively mobility. Its head end is the narrower and contains an oval aperture to which a canal is appended. This is at first narrow, but it then widens out and again contracts, ending below in an onion or pear-shaped swelling, the pharyngeal bulb. In the interior of this formation there is a small Y-shaped body with a lively movement that conveys the optical impression of three primitive teeth representing the chewing apparatus for the ingesta. An intestinal tube lined by a dark granular epithelium is joined to the bulb, and it terminates in an exceedingly fine canal above the very pointed tail end, the anus. Moreover, somewhat posterior to the centre and in a ventral position between the walls of the body and intestine a small lentil shaped body, the foundation of the still neuter sexual apparatus, may be recognised.

The embryos increase in size during the following days, becoming 700—800 μ in length and 24—27 μ in breadth, and then go through a process of moulting. The old sheath becomes loosened but does not fall off, and a clear watery substance is exuded between the old and the new sheaths; the former still, however, clings to the head and tail ends and lies close to the lateral surfaces of the worm. The movements of the creature are limited by this armature. Simultaneously other changes take place in the interior of the larva, the pharyngeal bulb disappearing.

Leichtenstern succeeded in keeping encysted larvæ alive in water for fully seven months. Embedded in moderately dry fæcal masses they also remain alive a remarkably long time, but the larvæ as well as the ova perish after being completely dried up.

Leichtenstern occasionally observed that the larvæ break open the armature and creep out of it, but soon after they again acquire another skin and become encysted a second time.

Looss, whose description of the history of development of anchylostoma varies somewhat from that of Leichtenstern, states that there are always two moultings.

Giles states that he cultured embryos on sand from the ova of anchylostoma, and from the embryos adult worms were produced which were different to other parasites inhabiting the intestine; these, moreover, deposited ova similar to those of anchylostoma. This experiment proves that it is possible to propagate the parasite outside the human body. Giles is of opinion that the anchylostomum has two different forms of development similar to those exhibited by rhabdonema strongyloides (see below). Probably his cultures may in some manner have become contaminated with other nematodes.

The anchylostoma invade the human intestinal canal in their larval condition.

On the grounds of experiments made on his own person, Looss is of opinion that the larvæ are able to enter *the body by the skin*, whence they probably make their way to the bowel by some unknown channel, and there attain puberty.

ETIOLOGY.

Infection by anchylostoma takes place by way of the stomach and intestine. From what we know of the conditions of life of the parasite, *water* or *moist solid materials*, are the media of transmission.

Favourable opportunities for the propagation of the disease are afforded in places where, in consequence of there being no latrines, excrement in large quantities is deposited in the vicinity of human habitations, or, as is the case in mines and brickfields, it is deposited near the dwellings of the labourers. The danger is still further increased if the soil be of soft clay, packed by being much trodden on, or on which domestic animals live, and where there is not sufficient drainage to carry off the rainwater; these conditions are particularly prevalent in the less civilised countries. It can be easily understood that under these circumstances, the people who live in such environment by various means, such as going bare-footed and afterwards washing their soiled feet, using dirty utensils, wearing soiled clothes, &c., contaminate their hands and get the encysted larvæ beneath their nails, whence they find their way into the mouth. This is most apt to occur in labourers who eat their meals on the spot, and convey the food to their mouths with hands that have not been thoroughly washed. This mode of infection is particularly likely to occur in children, especially such as are not very steady on their feet; as at one moment they may have their hands on the soil and at the next moment in their mouths; they may even choose earth, clay, or sand, to play with. The larvæ may, moreover, be washed by the rains from the polluted soil into water used for drinking purposes, thus forming another source of infection.

Transmission cannot take place by means of dust, as has been asserted by v. Schopf and others, for, as mentioned above, dried up larvæ perish very quickly.

As Leichtenstern has proved by experimentally giving food contaminated with larvæ to human beings, the larvæ pass unchanged through the stomach; their capsule becomes loosened in the intestine, and in this situation, after actually shedding their skin, they develop to adult anchylostoma. In the fourth week after infection Leichtenstern found the worms had not yet attained puberty, the females having no ova and the males no developed spermatic elements. Copulation takes place in the fifth or sixth week, and the ova are removed from the body with the intestinal evacuations of the host.

Looss has studied the development of anchylostoma in the intestine of the dog where they go through two further *processes of moulting*. After the first moult they are provided with a provisory oval capsule, but after the second with a definite one. From the period of the introduction of the larvæ until the adult form is attained four or five weeks elapse.

The disease may attack *either sex* and *every age*. Infants of the tenderest age are even attacked.

There is no racial predisposition. It is true that the disease mostly occurs in the coloured races, but this circumstance is attributable less to the peculiarities of race than to the unfavourable hygienic conditions under which they live.

Zinn and Jacoby assert that *negroes* are immune to anchylostomiasis to such a degree that it presents a racial peculiarity. In twenty-one out of twenty-three negroes from East Africa, West Africa, and Guinea these authors found ova of anchylostoma in the stools; in several in such great numbers as to lead to the belief that an enormous quantity of worms must have been present. In spite of this fact none of these negroes exhibited the symptoms of anchylostomiasis. The proof of this immunity is, however, not very striking, as the observers gave no further information as to the number of anchylostoma in the intestines of these negroes. It is also a remarkable circumstance that in the two cases in which extractum filicis was administered as a vermifuge, the result was completely negative. The conclusion is therefore arrived at that there was only a small number of worms, for if many

hundreds of anchylostoma were present in the intestine, such a therapeutical failure would be a very rare occurrence. Leichtenstern came across dozens of cases in his practice ; one person harboured 50—100 anchylostoma without exhibiting any remarkable symptoms of anæmia. As the natives in various countries suffer from severe anæmia in consequence of anchylostoma, it would be miraculous if the negro race alone formed the exception.

The disease is observed more frequently *in the country* than in towns, and persons whose *occupations* necessitate their working in damp soil, such as agricultural labourers, gardeners, ploughmen, brickmakers, bricklayers, miners, street-sweepers and cleaners of privies, are principally attacked, a circumstance easily accounted for.

SYMPTOMATOLOGY.

Many persons harbour a small or moderate number of anchylostoma and do not suffer from the slightest indisposition. According to Leichtenstern, the general health only deteriorates when hundreds of worms (at least 300—400) are harboured.

Anchylostomiasis is attended by signs and symptoms of more or less severity. *Anæmia* is one of the most pronounced of the accompanying conditions, and with it marked *disorder of the digestive organs.*

The anæmia is primarily attributable to the blood lost by the patients. This is caused, not only by the blood actually imbibed by the anchylostomes, but by the continuance of the bleeding from the leech-like wounds after the parasites have relinquished their hold. Besides the immediate loss of blood, two other conditions conduce to cause anæmia ; firstly, the digestive disorders from which the patients suffer in consequence of the morbid condition of the stomach and intestine, and secondly, an intoxication set up by a virus given off by the parasites. The discrepancy between the small number of worms and the severity of the anæmia is accounted for by such an intoxication, and it explains also the anæmia occurring not only in chronic cases in which formerly there was a large number of parasites that have decreased in course of time, but in fresh cases also. Perhaps, also, as in the case of the Bothriocephalus, the virulence of the anchylostomum is different locally and periodically. There is, however, no proof to justify such a conjecture.

The hypothesis of the generation of a toxin is supported by Lussana's investigation. This author confirmed the presence of *toxins* conducing to anæmia in the *urine* of *persons* suffering from anchylostomiasis. He condensed the urine at 60—70° to the thickness of syrup, extracted the residue with pure alcohol, and dissolved the extract after evaporating the alcohol in a little sterilised water. With this solution he subcutaneously injected rabbits for eight consecutive days, and thereby induced a loss of colour of the red blood corpuscles, poikilocytosis, and increase of fibrin. After the discontinuation of the injections these symptoms rapidly disappeared. Urine condensed in the same manner as mentioned above, but freed from parasites, caused no disorders in the rabbits. Lussana's observations have been confirmed by Arslan, but on the other hand not by Aporti.

Bohland, in two cases of anchylostomiasis, observed an *increase of decomposition of albumen*, which he attributes to the effect of a protoplasmic virus, engendered by the parasites.

The toxin hypothesis is, moreover, supported by the retinal hæmorrhage that sometimes occurs in anchylostomiasis, as well as by the proportion of the *hæmoglobin constituents*, to the number of blood corpuscles.

The *commencement* of the disease may be fairly acute if a large number of larvæ enter the stomach at the same time ; as a rule, however, the disorder starts insidiously, the introduction of the larvæ occurring gradually.

The patients gradually become pallid, tire quickly, and complain especially of digestive and intestinal disorders.

As a rule there is a gnawing or a feeling of throbbing, weight and discomfort *in the region of the stomach*. There is frequently tenderness *along the course of the intestine*, more particularly in the right and left hypochondriac regions. The pain is described sometimes as darting, sometimes as twitching, burning, cutting or dull; in rare cases it is increased by pressure, or it may be felt only when the part is palpated.

The *appetite* at the commencement of the illness is frequently increased to actual bulimia. In other cases, especially during the later course of the disease, it is decreased to absolute anorexia. Sometimes there is more or less eccentric desire for unripe fruits, green maize, acid foods, &c., or a great longing for such substances as cement, burnt clay, chalk, wood, coals, woollen material, paper, feathers, &c. As already mentioned, the disease has therefore been designated *geophagia* or *allotriophagia*, but this symptom is by no means peculiar to anchylostomiasis, but occurs in ordinary chlorosis, in pregnancy, as well as when any intestinal worms are present. Through the alkalies contained in the earth, the acids of the stomach are neutralised, and the digestive disorders of the patients are relieved (Prowe). Geophagia is noticed particularly in children.

Geophagia, which is often a symptom of the illness, may also be a cause of the disease, for in many of the countries in which anchylostomiasis prevails, eating earth is customary. Sandwith reports that in Egypt the fellahs, more particularly women, frequently eat earth and slime from the Nile, presumably on account of an ancient superstition that Nile slime, having so fertilising an effect on vegetation, also proves salutary to the human body. On the day on which the Nile rises to its maximum, Nile slime with citrons is offered for sale in the streets, and is freely bought and eaten.

In the Indian Archipelago, certain kinds of earth called *ampoh*, is frequently eaten by pregnant women, in the belief that it benefits the still unborn child. It is eaten partly dried, partly baked. The chemical examination of these kinds of earth only reveals inorganic constituents with tarry clay, so that they may be regarded as quite worthless for food (van der Burg). In the coal mines a sort of slate is eaten, that undoubtedly has poisonous properties, and if its use is long continued, may cause death; the poisonous constituent of this material, however, has not been found. According to Altheer, the reason for dirt-eating is that the bituminous argillaceous earth contains air in its numerous pores, which originates an agreeable stomachic sensation (van der Burg).

Various South American races of Indians, especially the *Otomakes*, on the Orinoco, are notorious eaters of clay. In New Caledonia the natives eat large quantities of a greenish soap-stone, not only when they are hungry, but even after hearty meals.

The following disorders are also frequently complained of by the patients: Heart-burn, a sensation of weight after eating, eructations, nausea and vomiting. Sometimes even blood is brought up in larger or smaller quantities. The epigastric region is frequently distended with wind, the tongue whitish and coated with slime, and there is increase of the secretion of saliva. Goldmann frequently observed *ulcer of the stomach*, a condition which would still further tend to produce anæmia; Leichtenstern, in chronic cases, occasionally observed at autopsies a *dilatation of the stomach* associated with an atonic and thickened condition of the wall, with a lack of hydrochloric acid in the gastric juice; in exceptional cases also he found an arrest of gastric secretion.

Constipation usually obtains, but in far advanced cases diarrhœa or even dysenteric symptoms may prevail.

The stools are often of a peculiar, dirty, brownish-red colour, due to the presence of altered hæmoglobin. Some observers describe them as colourless and poor in bile. Leichtenstern found that the fæces of brickmakers were discoloured to a greyish-yellow tinge in consequence of their

clayey contents. In the later stages the intestinal evacuations contain undigested food, and slime and blood. The mucus is seen partly coating the fæces and partly in the form of large or small lumps. The blood is either mixed in larger or smaller quantities with the mucus, or large quantities of liquid blood are evacuated. According to Leichtenstern, bloody stools are also frequent in fresh cases, especially when the invasion of the larvæ is sudden and in great numbers ; in older cases, on the other hand, blood in the stools is hardly ever observed.

It is only quite exceptionally that dead anchylostoma are spontaneously passed at stool. On the other hand, the ova are often found in the fæces in great numbers. According to Leichtenstern, four million ova in one stool are not unusual. They are usually evenly distributed in the fæces, and are easily discovered by the microscope.

The number of *anchylostomes contained in the intestine* can be approximately computed from the number of ova in the stools ; according to Grassi and Paroni, 150—180 ova in 1 cg. of fæces correspond to 1,000 worms, *i.e.*, 750 females and 250 males.

According to Leichtenstern the number of females ($\times$) can be computed by the number of ova in 1 g. fæces (*a*) divided by 47 ($\times = ^a$). Loose stools are not suitable for such reckonings.

Charcot-Leyden's crystals, although not a constant constituent of the stools are nevertheless frequently present. These crystals are not pathognomic of anchylostomiasis, for they are also found when the anguillula intestinalis or other intestinal parasitic worms occupy the intestine. These crystals are also found in the sputum when pulmonary parasites, such as echinococcus and distomum pulmonale, are present.

Leichtenstern, during his experiments on the effects of foods, found that the *Charcot-Leyden's crystals* appeared in the third week after the ingestion of the larvæ, and that the first ova of anchylostoma appeared eight days later in the stools.

Charcot-Leyden's crystals are probably a product of the parasites. Leichtenstern, at autopsies, found them in greatest quantity in the intestinal mucus, at the spots where the parasites had their seat, and they disappear entirely from the stools after complete expulsion of the parasites. The *increase of the eosinophile cells in the blood* has probably some relation to their toxic effect on the blood, analogous perhaps to the absorption of the toxins of bacteria. After successful treatment by means of vermifuges the number of eosinophile cells slowly returns to normal (Bücklers).

Prowe states that he almost always found dark brown or blackish rhomboid hæmin-crystals in very large numbers ; this observation remains unconfirmed by other observers.

Lutz occasionally observed *circumscribed peritonitis* with very slight general disturbance. The intestines in consequence may become covered by an effusion of lymph which, although it causes some temporary obstruction and knotting of the bowel, usually disappears in a few weeks when suitably treated.

Next to the digestive symptoms, *disorders of the circulation* play the most important part in the symptoms of the disease. The patients frequently complain of *palpitation of the heart*. At first this is only observed after severe exertion ; but later on it sets in when the patient is doing light work, or experiences some emotion, and in severe cases it even occurs during rest. The patients also sometimes complain of palpitation in the epigastric region. The palpitation of the heart is frequently accompanied by shortness of breath and sensations of pain, which are described as being darting, or burning, or sometimes as a dull pressure. These pains have given rise to the disease being designated *mal de cœur*. Lutz ascribes this sensation of pain, as well as the pains in the limbs to be mentioned below, to a sense of fatigue, the result of the accentuation

and acceleration of the action of the heart. The pulse is accelerated, easily excited, occasionally intermittent or irregular, the impulse of the heart is unusually strong. There is in some cases hypertrophy of the heart, particularly observable in the left ventricle. Anæmic cardiac murmurs, as well as *bruit de diable*, are frequent symptoms. Actual endocarditis and valvular disease have also been observed. Dropsy sometimes sets in ; the cheeks, eyelids, the dorsal aspects of the hands and feet being most usually swollen ; in bad cases ascites, hydrothorax, and more rarely, cerebral œdema occur.

The blood, even macroscopically, appears considerably paler than normal. Microscopical examination of the blood shows that the red corpuscles are diminished to two or even one million in the c.b.m.m. and even to less. There is also a fair degree of poikilocytosis and microcytosis. The proportion of the leucocytes to the red corpuscles is at first normal ; later on the white blood corpuscles are increased. Masius and Francotte cite a case in which a leukæmic condition of the blood developed during the last stage of the disease ; the white blood corpuscles were of various sizes ; the so-called bone-marrow cells were also present in larger numbers than normal. Various observers (Müller and Rieder, Zappert, Bücklers) incidentally discovered numerous eosinophile cells.

The decrease in the hæmoglobin is not parallel with the decrease of the number of red blood corpuscles, but even exceeds the latter in diminution. Sandwith found coincidently, that, while the number of red blood corpuscles most frequently averaged between two and three millions per c.b.m.m., the hæmoglobin contents averaged 26 per cent. (This observation is confirmed by Gowers.)

The *skin* of patients in whom the disease is far advanced is livid, pallid, with a yellowish tinge, resembling the appearance of the skin in malarial or cancerous cachexia. Actual icterus, however, is exceedingly rare (Sandwith). Occasionally, the cutaneous pigment is increased ; not only does the colouration partake partly of the nature of an ephelis, but chloasma obtains and occasionally the entire skin is more pigmented than usual (Lutz). The skin of the coloured races becomes lighter from the effects of the anæmia ; in negroes, particularly, it becomes grey, or ashen grey, and withered, dry, lustreless and exfoliating.

The *mucous membranes* as well as the skin, are pale.

The remaining symptoms to be noted in persons suffering from anchylostomiasis are all more or less direct consequences of anæmia, and appertain for the most part to the nervous system. There is headache, tinnitus aurium, darkening of the field of vision, giddiness, swoons, weakness, fatigue, sleepiness, apathy, a tendency to shiver. In addition to these, there is, moreover, formication and " falling asleep " of the limbs, also pains in various parts of the body, particularly in the legs. Sandwith, in 48 per cent. of his cases, observed absence of the patellar tendon reflexes ; in 5 per cent. of cases the reflexes were diminished and in 12 per cent. of cases increased.

A few observers, such as Grassi, Fischer, Nuel and Leplat, mention the occurrence of retinal *hæmorrhages* and *neuro-retinitis,* Leichtenstern observed the occurrence of *pains in the bones,* more particularly in the sternum.

The *urine* is often copious and pale, rarely albuminous. Völckers always observed a more or less increased indican reaction.

De Renzi always found *peptonuria* and *urobilinuria* as a consequence of the hæmolytic effect of the toxins of the anchylostoma.

As to the *sexual functions*, severe anchylostomiasis in men causes impotence, and in women menstruation ceases. Conception seldom takes place except in mild cases of the disease and the infants are born in a miserable atrophic condition (Wucherer). The growth of young adults is seriously interfered with by the presence of a large number of anchylostomes in the intestines.

The disease may lead to extreme emaciation; but on the other hand, *nutrition* is not disturbed, and the fat of the body is even well developed.

The *temperature* in mild cases is mostly normal; in severe cases it appears on an average to be a few points lower; in such cases, also, as in pernicious anæmia, evanescent rises of temperature are observed (anæmic fever). Giles and Sandwith often observed fever, which, however, was only observable for a few days, at the commencement of the illness. The same symptoms occurred in monkeys that had been fed with the larvæ of anchylostoma.

Pleurisy with some effusion (even without tuberculosis) was a *complication* observed by Leichtenstern with remarkable frequency, and the same authority states that chronic nephritis occurs as a concomitant of anchylostomiasis.

The *duration* of the disease varies considerably and may fluctuate between some weeks and several years, ten or even twenty years.

There may be spontaneous *recovery*. When recovery takes place, if the patient is removed from the possibility of further infection, the worms gradually die off and are evacuated. The natural period of life of the anchylostomum appears to be at most five years according to Leichtenstern's computation; in any case, however, it does not exceed eight years.

If the parasites are expelled, the recovery is remarkably quick; in young people, one to three months may suffice, provided that irreparable damage has not already been caused by the disease. If the parasites are not expelled, the disease progresses and death may result through exhaustion, extensive dropsy, and profuse diarrhœa; or the end may be hastened by intercurrent diseases such as pneumonia, tuberculosis, malaria, beri-beri and other illnesses.

PATHOLOGICAL ANATOMY.

The bodies of persons who have succumbed to anchylostomiasis are usually more or less emaciated; in some cases, however, the adipose tissue is remarkably well developed. Œdema is frequently present, and there may be accumulations of fluid in the various serous cavities and œdema of the cerebral meninges.

All organs are distinguished by *great pallor*.

The *lungs* are usually œdematous.

The *heart* is often hypertrophied, particularly the left ventricle, and the myocardium is relaxed, very pale and of a more or less distinct yellow tinge in consequence of fatty degeneration; occasionally, especially in the papillary muscles, there is intense signs of degeneration (Grassi), in addition to general, moderate, fatty degeneration.

The *liver* is slightly fatty; in rare cases amyloid degeneration is observed.

The *spleen* in uncomplicated cases is normal or shrunken and atrophic; it is seldom amyloid.

The *kidneys* are mostly very pale, slightly fatty, seldom amyloid. According to Wucherer, Brazilian doctors found the pancreas enlarged.

The *stomach* sometimes presents the appearance of chronic catarrh; in isolated cases it is much dilated.

The *jejunum* and *ileum* are the seat of numerous petechiæ the size of a lentil; they may be partly fresh and dark red, and partly old and slate-coloured. In acute cases of anchylostomiasis the mucous membrane is dotted with fresh hæmorrhages, whereas in cases of longer standing, even when enormous numbers of worms are present, only a few hæmorrhages may be seen. To many petechiæ a worm is often found attached. In others, the deepened centre, in which a solution of continuity of the mucous membrane is seen, points to the fact that anchylostoma formerly had their seat there. As already mentioned, there may be hundreds or even thousands of worms, and the number of deserted " seats " may far exceed the number of clinging worms found. In autopsies carried out some time after death portions of the anchylostoma may be found loose in the intestinal mucus.

Several authors cite cases of larger hæmorrhages in the sub-mucosa also. Bilharz and Grassi found anchylostomes coiled up in these blood-filled spaces, and in Grassi's case the worms were still small and undeveloped. On account of this discovery the authors sought to prove that there was a submucous stage of development of the anchylostoma preceding their free life in the intestinal lumen. The most probable explanation, however, is that these worms had strayed and bitten the mucous membrane through. Sandwith sometimes found half of the bodies of anchylostoma bored into the mucous membrane.

Especially in fresh cases sanguineous or chocolate-coloured contents are found in the intestines, and the mucous membrane is thickened. Swelling of the solitary follicles and Peyer's patches has also been observed, as well as enlargement of the mesenteric glands. Prowe found the latter enlarged to the size of filberts in three fourths of all his cases, and rosy on section. One of the cases observed by Williams, in which death ensued from perforation of the jejunum and in which a number of annular cicatrices were present in the duodenum and jejunum demonstrated that anchylostoma probably also lead to intestinal ulcerations.

Wucherer found adhesive peritonitis, and Masius and Francotte, in one case, found the same changes in the bone marrow as are met with in pernicious anæmia; the marrow showing a greyish red colour in the long bones with loss of fat. Numerous medullary cells and nucleated red blood corpuscles were observed in the marrow.

DIAGNOSIS.

The diagnosis of anchylostomiasis is founded on the microscopical demonstration of the *ova* of *anchylostoma in the stools of the patients.* They may be easily recognised and distinguished from the ova of other intestinal parasites. It is possible perhaps to confuse them with the ova of the *oxyuris vermicularis*, but even this mistake can be avoided if one remembers that the latter are smaller (52μ in length and 24μ in breadth) that they are unsymmetrical, being more curved on one side than on the other, that they have a thin but doubly outlined shell, and that they contain an embryo which is already developed and possessed of lively movements.

For examination the smallest possible portion of fæces is removed with

a needle and spread out as a thin layer on a slide. If the stools are hard a little water is added, but this is unnecessary if the stools are pulpy or thin. If the result of the examination is negative a purgative is given, after which often, even when but few anchylostoma are present, many ova are passed. Sandwith recommends, when there is continued suspicion of anchylostomiasis, notwithstanding the circumstance that no ova are found in the fæces, that experimental cultures should be made with the stool. The presence or absence of the parasite will then be proved with certainty.

The examination of the stools differentiates anchylostomiasis from *chlorosis, pernicious anæmia, malarial or cancerous cachexia, cardiac affections*, &c., these ailments having some points of resemblance with anchylostomiasis.

Rogers recommends the examination of the blood for the differential diagnosis between anæmia of anchylostomiasis and malarial anæmia. In malarial anæmia the hæmoglobin and the red blood corpuscles are diminished to an equal or almost equal degree; the colour index is about normal $= 1$. In the anæmia of anchylostomiasis the hæmoglobin is diminished twice as much as the red blood corpuscles, the colour index $= 0.5$. The white blood corpuscles in malaria are relatively more diminished than the red $(1 : 1,000—2,000)$; in anchylostomiasis, on the other hand, they are relatively increased $(1 : 300—400)$. The specific gravity of the blood in proportion to the degree of the anæmia in anchylostomiasis is more diminished than in malaria. In complications of the two diseases the blood examination is of value in order to discover which predominates; an unusually low colour index proves the presence of a large number of anchylostoma.

If in a severe case of illness only a few ova are found, the question of complications must be considered. But it may be that the worms, which at first were present in great profusion, have gradually diminished in numbers till only a few are left in the intestine, and yet the disorders caused by the parasites have not disappeared, the ravages being irreparable.

PROGNOSIS.

The prognosis of anchylostomiasis is in general favourable, owing to our knowledge of means by which the parasites may be expelled with certainty. It is only when the complaint has already made great strides that one cannot rely on recovery; Sandwith, who has reported on more than 400 cases, succeeding in curing entirely or producing considerable improvement in 89·5 per cent. of his patients; 2·5 per cent. were not relieved and 8 per cent. died.

PROPHYLAXIS.

In order to avoid the disease, measures must be taken to put an end to the unhygienic conditions which prevail in some countries where the anchylostomum prevails. Where latrines are wanting they should be erected, and the fæces deposited in these alone. It is also advisable to cover the contents of the latrines daily with some soil with the object of destroying the larvæ, which require air for life; or the stools of the patients may be made harmless by disinfectants (chloride of lime, 10 per cent. sulphuric acid, 2 per cent. sublimate).

Giles advises the ploughing of infected areas in order that the embryos may be buried.

As anchylostomiasis may be carried by patients and thus form new centres of infection, it is necessary to examine labourers who are to be employed in carrying out large earth-works, erecting fortifications, building tunnels and canals, or employed on brickfields, or in mines; and if it is found to be necessary, purgatives should be administered. It is also advisable to examine Europeans returning from warm countries, particularly if they are anæmic.

Individuals must be warned to avoid infection by the most scrupulous cleanliness. Hands soiled by labour must be thoroughly washed before each meal. One should also avoid drinking polluted water. Suspected water, when pure is unobtainable, should always be boiled or filtered before use.

TREATMENT.

Treatment has a twofold mission (1) *the expulsion of the parasites*, and (2) *the relief of the anæmia set up by the presence of the worms.*

Two drugs have proved particularly useful, as vermifuges, *extractum filicis liquidum* and *thymol (acidum thymicum, thymolicum)*; nevertheless anchylostoma exhibit a most remarkable power of resistance, even to these drugs.

Extractum filicis is, as in tape-worm treatment, administered in gelatine capsules (up to 0·5) or with an equal or double quantity of syrup or brandy, to which 15 drops of chloroform may be added to prevent vomiting (Brölemann).

Leichtenstern advises, and with this I agree, that 10·0 should not be exceeded. On the afternoon previous to the exhibition of the anthelmintic, a dose of calomel or some other aperient should be administered, and only a little light food given in the evening. The next morning a cup of black coffee is given to the patient and the capsules should be taken within half an hour, or the mixture, divided into two parts, given at intervals of half an hour. Two hours later a saline aperient is administered (Epsom salts, Carlsbad salts, or soda sulphate). The use of castor oil is to be avoided, as, according to recent investigation, the poisonous filicic acid is soluble in oily substances and absorbed very easily.

In the case of patients who are much reduced, Parona recommends smaller doses on several consecutive days (2·0—4·0).

Failures, as in the tape-worm treatment, are often attributable to the drug being of bad quality. (Unless quite fresh the filicic acid in the preparation gradually changes into an inefficacious filicic acid hydrate, which is deposited in crystals.)

According to Mosler and Peiper the failure of the drug to cure depends, not on the drug being ineffective, but on the bad state of the stomach and intestine. The effect undoubtedly is considerably less or even negative when there is a copious secretion of mucus and when the drug only reaches the duodenum slowly, than under more favourable circumstances.

The Italian doctors administer far larger doses of extract of male fern (20·0—40·0) but the fact that the extract prepared from the rhizome grown in Italy is much weaker in its effect than when obtained from the German plant must be borne in mind.

It is as well, however, not to exceed the usual maximum dose of 10·0 in adults, as after very large doses symptoms of poisoning often set in. In mild cases of poisoning by male fern icterus ensues, which, according to Grawitz,[1] may tend to cirrhosis of the liver; in moderately severe cases, violent vomiting, abdominal pain, a feeling of feeble-

Berl. Klin. Woch., 1894, No. 52, p. 1171.

ness, swooning and somnolence may occur, and occasionally also, amblyopia and amaurosis. In very severe cases cerebro-spinal paralysis may develop, and a fatal issue result within a few hours.

Thymol is exhibited in doses of 4·0—8·0 (Leichtenstern orders up to 10·0 or 15·0) in wafers or gelatine capsules. The day before the thymol is given, the patient must only eat light food, and in the evening take an aperient (calomel is the best); if necessary, an enema is given in addition. On the following morning 2·0 of thymol is administered four times at intervals of one hour and a half. The patient must keep his bed during the treatment. A light liquid diet is given (black coffee, bouillon, soups, milk), but no alcohol, in order to prevent the thymol, which is soluble in spirit, being absorbed by the intestine. Should free absorption of the drug occur, symptoms of poisoning may result, characterised by fall of temperature, retardation of the respiration and pulse, giddiness, collapse, or delirium. Any sensation of burning along the digestive canal and in the region of the stomach is relieved by ice or cold water. If no spontaneous stool follows, an aperient is given twelve hours after the last dose (sulphate of magnesia or castor oil).

Monari orders 3·0 of thymol to be taken on several consecutive days, and Leichtenstern, in ambulatory treatment, orders 20·0 to be divided and given in small doses for several days, namely, every morning two to three doses of 2·0 each at intervals of two hours.

After taking thymol the urine assumes an olive-green colour, which deepens if it is left standing.

Thymol is *contra-indicated* when there is a tendency to vomit, when there is great weakness, a very low temperature, in persons over 60 years of age, and in advanced cardiac or other organic diseases care should also be exercised. It should also be administered with great reserve in persons weak from anæmia, dysentery, or malaria. Leichtenstern, in one case in which he gave thymol, observed that acute nephritis set in which afterwards became chronic. Slight transitory albuminuria is frequently observed after both thymol and extract of male fern.

In *children* both drugs are administered in half doses or less, according to their age.

The vermifuges fail more frequently in recent than in the older cases of illness, the worms being then smaller, and therefore more easily able to conceal themselves between the folds of the mucous membrane, where they escape the effects of the drug.

In order to *find the anchylostoma in the stools*, Leichtenstern advises that the fæces be diluted with water, well stirred up and poured into flat dishes; large particles of the fæces should be broken up with the forceps, and the mass then carefully decanted; the worms are then left in the sediment.

If all the worms have not been expelled, a fact that can be ascertained by the continued presence of ova in the stools, the treatment must, if necessary, be repeated several times, but at no more frequent intervals than once a week, and no case is to be considered to be cured until ova can no longer be found after several examinations on consecutive days. Of course, if all the females have been removed, and only males are left, the latter being more difficult to expel, probably in consequence of their smaller size, no more ova will be exhibited in the stools. The presence, however, of Charcot-Leyden's crystals serves to confirm the existence of worms.

Sometimes after the treatment the ova disappear from the stool, only to again reappear after some time. The reappearance must be due either to the fact that the adolescent worms were not expelled and that they

subsequently became matured, or that some of the adult worms were not expelled but only made ill, thus interrupting ovulation; after recovery from the effects of the drug the parasite again resumed its natural functions. It is therefore always advisable to examine the stools of patients for ova after some time, even in cases of apparent cure.

The second indication, namely, the *cure of the anæmia*, is accomplished by good food, preparations of iron, &c. In severe cases Lutz recommends a systematic milk-cure. Very advanced anæmia may necessitate transfusion or infusion of common salt.

If the bowels are sluggish, saline aperients in moderate doses should be administered.

Digitalis is indicated to improve the action of the heart when there is severe dropsy, accelerated and irregular action of the heart, cyanotic tinge of the lips and nails, and decrease in the secretion of urine.

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VII.

RARER AND LESS IMPORTANT PARASITES.

1. DISTOMUM CRASSUM, Busk.

Synonyms: *Distoma Buski*, Lankester; *Distoma Rathouisi*, Poirier.

THIS worm, which was discovered by Busk in 1843, is the largest distomum hitherto found in man. It has, according to Braun (see fig. 48) a length of 4—8·5 cm. and a breadth of 1·4—2 cm. It is principally distinguished from distomum hepaticum by the fact that its intestines are not ramified. Its ova are 1·025 mm. in length and 0·075 in breadth; they are oval in shape, and provided with a lid.

It lives in the *intestine*, and probably also in the *liver* of man, and seems to cause *diarrhœa* and hepatic disorders.

The distomum crassum has hitherto been found in China, Selangor (Further India), the North West Provinces, Assam and Borneo, or in persons that have lived in these places.
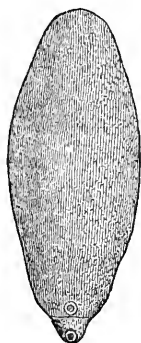
FIG. 48.—*Distomum crassum*, natural size. After Leuckart.

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2. TÆNIA NANA, v. SIEBOLD.

Geographical Distribution.

The *tœnia nana* was discovered by Bilharz in Egypt in 1852, and has been found besides in Servia, Italy, Sicily, where, according to Grassi, it is the most frequent tape-worm; it is also found in Philadelphia, Argentine, Brazil, Siam and Japan; recently, also, it has even been observed in Germany (Cologne).

Natural History.

The *tænia nana* (see fig. 49) is a small tape-worm which, according to Leuckart, is rarely more than 20 mm.[1] in length ; it is of a white or pale yellowish colour, and its greatest breadth does not exceed 0·5 mm.

The anterior portion of the body, to about the extent of a third of its entire length, is thin and thread-like, the body then spreads out towards the posterior part, the posterior third of the body being about the same breadth. The spherical head, which is 0·3 mm. in diameter, has four round sucking discs and a rostellum provided with a circle consisting of from 24 to 28 exceedingly delicate hooklets ; the rostellum can be thrust forward or retracted. The number of small joints averages 180—200, of which the last 20 to 40 contain mature eggs. The ova (see fig. 50), according to Mertens, are oval, of a fairly light whitish colour, and remarkably transparent. At their greatest axis they measure 47—48 μ on an average, and at their smallest axis, 38—39 μ. The shell consists of two membranes, which are divided from each other by an interstitial substance consisting of wide meshed filaments which, at the extremities of the ovum averages 9—12 μ, and at the centre 6—8 μ. The embryo, which is almost spherical, is 20—25 μ in diameter, and is provided with hooklets 6—10 μ in length.

Fig. 50. — Ovum of *tænia nana*, enlarged 600 times. After Mertens.

The *small intestine* constitutes the habitat of *tænia nana*, and this is particularly the case with *children*, where they burrow deeply in the mucous membrane. It is not uncommon for one intestine to shelter thousands of these parasites. According to Grassi and Lutz *tænia nana* is identical with the tænia murina, (Dujardin), of the rat and mouse, which goes through its cystoidal stage in the intestinal mucous membrane of the definitive host. According to this authority infection is conveyed direct by means of the ova ; v. Linstow, however, disputes the identity of the two parasites.

Fig. 49.—*Tænia nana*, enlarged 18 times. After Leuckart.

Symptomatology.

When the great number of parasites which often are sheltered by one person is taken into consideration it is not surprising that these worms

[1] The longest parasite observed by Mertens measured 3·25 cm. without the head, which was not found.

are of pathological importance. The disorders originated by them consist partly of symptoms of *chronic intestinal catarrh* and partly of serious *nervous affections*. The intestinal symptoms consist of abdominal pains, constipation, alternating with diarrhœa, perverted appetite, bulimia and emaciation. The nervous symptoms are attributable either to mechanical irritation exercised by the parasites by reflex action, or originated by a virus generated by them; they consist of insomnia, spasmodic movements, epileptiform attacks without loss of consciousness, weak memory, melancholia, &c. Accompanying these symptoms dyspnœa and asthmatical attacks have been recorded, and Lutz also observed irregular attacks of fever in two cases.

The fact that these symptoms are actually caused by the parasites is proved by the circumstance that they disappear after the expulsion of the worms.

Diagnosis.

The diagnosis of tænia nana is grounded on the demonstration of the ova in the stools. These ova are so characteristic in appearance that they are easily differentiated from those of other tape worms, especially from those of tænia solium and tænia medio-canellata, both of which have a brown shell with radiating lines.

Treatment.

Extractum filicis liquidum is recommended therapeutically; but inasmuch as most of the patients are children, to whom large doses cannot be administered, the treatment is defective, the worms being mostly expelled without heads so that repeated treatment is necessary. If some of the parasites remain unexpelled, ova will again be observed in the stools after about a fortnight. Santonin and thymol have proved inefficacious.

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3. BOTHRIOCEPHALUS LIGULOIDES, Leuckart.

Synonyms : *Ligula Mansoni*, Cobbold ; *Bothriocephalus Mansoni*, Blanchard.

The Bothriocephalus liguloides (see fig. 51), which has hitherto only been observed as a larva, attains, according to Leuckart, a length of 20 cm., or even more, with an average breadth of 2·5 mm.   It is of a faint white colour, and has a tape-like jointless body of fleshy consistence, which becomes narrower towards its posterior part.   Anteriorly the body widens out and supports a papilla-like projection, on which the piercing apparatus and more or less stippled head, provided with two suctorial discs, is situated.   Sexual organs are entirely absent, and nothing is known of its development and origin.   It is conjectured that a domestic animal is the host of the definitive worm.

The parasite was found first by me in Japan in 1881, and in the following year by Manson in China (Amoy), and since that time a number of cases have come under observation in Japan.   Other homes of this parasite, however, have not become known.

The *subperitoneal connective tissue* appears to be the natural habitat of the larvæ, especially in the vicinity of the kidneys, where it was found by Manson whilst performing an autopsy on a Chinaman who died of dysentery and stricture of the œsophagus.   From the subperitoneal tissue the worm may *migrate*, and reach the urinary passages, the pleural cavity (as in Manson's case), or it may even appear through the skin.   Of the total ten cases hitherto observed it has been twice found at autopsies ; four times it has been passed in the urine or extracted from the urethra (as in my case) ; it has been removed in three cases from a swelling in the vicinity of the eye ; and it has once been extracted from the subcutaneous connective tissue of the lumbar region.

The invasion of the urinary passages by the worm is followed by retardation of micturition, and by pains in the urethra and vesical region which radiate to the

a   b

Fig. 51.—*Bothriocephalus liguloides*.   Natural size. *a*, My specimen ; *b*, after Cobbold.

thighs. Hæmaturia has also been observed, the symptoms persisting until the parasite was got rid of.   It is therefore incumbent on the medical man, in countries where this worm is found, to consider the possibility of this cause when treating patients with such symptoms.

In my cases the urinary affections were preceded for some time by swelling and pains of the left testicle, a diffuse induration of the skin of the upper portion of the left thigh, as well as pains in the left inguinal region which radiated from thence to the hypochondrium ; these advanced symptoms disappeared, but they were probably attributable to the parasites.

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4. FILARIA LOA, GUYOT.

Synonyms: *Filaria oculi*, Gervais and van Beneden; *Filaria subconjunctivalis*, Blanchard; *Filaria lacrymalis*, Dubini; *Dracunculus oculi*, Diesing; *Dracunculus loa*, Cobbold.

Geographical Distribution.

The West Coast of Africa, especially Guinea, is the local habitat of this parasite, which was discovered by Bajon in Cayenne in 1768. From thence it was carried with the negroes to South America and the Antilles, but, since the importation of negroes has ceased, it no longer occurs there.

Natural History.

The *filaria loa* is a thread-like white or yellowish worm of the thickness of a fine violin string. The *female* is 30—40 mm. long, and rarely attains the length of 70 mm. The *male* is shorter, 16—22 mm. in length, or somewhat longer. The anterior extremity is rounded and blunt, the posterior end is pointed, the mouth has no armature, but is somewhat protuberant, and the intestine straight. The caudal end of the male is bent, and possesses five large papillæ on either side of the anus, and is provided with two somewhat short and uneven spiculi. The uterus of the female is filled with ova 35 μ in length and 25 μ in breadth, which quite early contain embryos.

The history of the development of the worm is unknown. Manson formerly conjectured that the filaria diurna was the parent worm, but appears to have relinquished this opinion, as in one case of filaria loa he was unable to find embryos in the blood and in another case Robertson's experience was similar.

The parasite appears to have a long life, for it sometimes comes under observation ten years, or even longer, after the patients have left the endemic district.

It lives in the cellular tissue under the skin and conjunctiva.

Symptomatology.

Filaria loa is observed in various parts of the body, but more particularly in the *eyelids* and beneath the *conjunctiva*. It is possible occasionally to follow the lively movements of the worm in its migrations through the cellular tissue. The motions are particularly lively in the warmth (in warm weather, in a warm room, in front of the fire), whereas it retires into the depths in the cold. It causes itching or stinging and a sensation of creeping, with a circumscribed redness and swelling on the places affected. When, however, it attains the sub-conjunctival cellular tissue it is especially prone to originate severe symptoms of inflammation (redness, swelling, flow of tears, itching and shooting pains), and which when situated at the inner angle of the eye, bear some resemblance to those of

dacrocystitis. It may also penetrate to the anterior chamber of the eye, as the case observed by Coppez and Lacompte proves. Sometimes it migrates from one eye beneath the skin at the root of the nose to the other eye ; Roth also believes that it sometimes attains the nasal canal and is then either swallowed or spat out.

Probably the so-called *Calabar swellings*, which come under observation on the West Coast of Africa amongst negroes as well as whites, and which appear on the most diverse parts of the body, may be attributable to filaria loa. These swellings originate suddenly, attain about the size of half a goose's egg, and then generally disappear in the course of three days. They are painless, firm, somewhat hot—objectively as well as subjectively—and do not pit on pressure.

Predtetschenski (Moscow) in one case of *chyluria* found ova in the urine, which resemble the ova of tænia nana.[1]

Treatment.

The treatment consists in the *removal of the parasite*, which, however, is often a very difficult matter on account of its rapid movements. Should it be situated beneath the conjunctiva, the eye should be cocainised, the globe steadied by the finger, a fold of the conjunctiva over the worm raised by forceps and incised by scissors, when the worm can be extracted by means of an iris forceps.

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5. PENTASTOMUM CONSTRICTUM, v. SIEBOLD.

Synonyms : *Nematoideum hominis*, Diesing ; *Linguatula constricta*, Blanchard ; *Porocephalus constrictus*, Stiles.

Pentastomum constrictum, discovered by Pruner in Egypt, has hitherto only been seen in its larval condition. It is from 13—22 mm. in length

[1] *Rusz Arch. der. Path.*, viii., No. 6 ; *Ref. Lancet*, 1900, March 3, p. 637 ; *Ztschr. f. klin. Med.*, xl., Nos. 1 and 2.

and on an average 2—3 mm. in breadth (see fig. 52a). It is of a milky-white colour, vaulted on the back and flattened on the abdomen, the head is broad and blunt, and the worm gradually narrows off becoming smaller towards the tail. There are four symmetrically placed golden-yellow movable hooklets in the vicinity of the oral aperture. The entire body is composed of rings, which are particularly perceptible when the creature moves; the rings are divided by constrictions which, according to Gerard, number 16 to 20. The parasite has hitherto only been found in *African negroes*. It is found partly rolled up in roundish *cysts*, each containing one parasite only (see fig. 52 *b*) in the *liver*, in the *mesentery*, under the mucous membrane of the *small intestine* and in the *lung*, partly free in the *abdominal cavity* and in the *small* intestine.
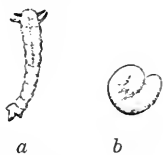
a   b
FIG. 52.—Pentastomum constrictum. After Pruner: *a*, free; *b*, rolled up in a cyst.

Pruner found the pentastomum constrictum in the giraffe also.

The natural history of the parasite is still unknown. It probably by some means gets into the intestine, thence gains entrance to the liver in which the cysts originate from dilated biliary ducts, and attains the peritoneum. The lungs seem to become infected by way of the trachea, and here the cysts are formed from dilated bronchioles. The parasite induces no serious disorders in the intestine and liver; if, however, it reaches the *peritoneum* and lungs it may originate serious *inflammatory symptoms* leading to a fatal termination.

In one case, which was confirmed by Gerard, death ensued in consequence of *purulent meningitis*, which originated from suppuration of the left frontal sinus. Perhaps this condition had been introduced at one time by a parasite which had subsequently been expelled from the body by sneezing or some such process.

When negroes exhibit disorders of this nature, pentastomum constrictum should be considered as a possible cause.

The diagnosis is established by the examination of the fæces for the presence of the parasite.

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6. THE SAND-FLEA. (Chigger.)

Synonyms : *Pulex penetrans*, Linné ; *Sarcopsylla penetrans*, Westwood ; *Rhynchoprion penetrans*, Oken ; *Dermatophilus penetrans*, Guérin ; *Chigger ; Chique ; Chigue ; Chego ; Tschike* (Antilles) ; *Djigga* (Congo) ; *Sikka* (Guiana) ; *Bicho, Tunga, Jutecuba, Migor* (Brazil) ; *Nigua* (Mexico, Nicaragua) ; *Pieque* (Paraguay).

Central and South America, from Mexico to Argentine, is the home of

the sand-flea. A ship carried the insect from Brazil to the West Coast of
Africa in 1872, first of all to Ambriz, south of the Congo ; it here spread
with incredible rapidity, so that at the present time it is distributed over
a large part of this quarter of the globe. Lately it has appeared in
Madagascar, India (Bombay, Karachi) and Further India (Penang),
having been carried to these places from Africa. In Ningpo (China)
Blandford observed that the chigger infested rats.

In all countries dry, sandy soil, the dirty dusty huts of the natives, and
the stalls of animals—more especially pig-styes—are the principal abodes
of this parasite. It infests all warm blooded animals, and is a great
nuisance to the *natives*, whereas Europeans, wearing shoes, are fairly safe
from infection.

The sand-flea (see fig. 53) is from 1 to 1·2 mm. in length, being about
half the size of the common flea, and is of a brown colour. The males
and the unimpregnated females, like the ordinary fleas, only transiently
seek human beings in order to feed on their blood. The *pregnant females,*
on the other hand, *burrow into the skin with their heads,* their presence
being manifested as a black speck resembling an embedded splinter ;
easily recognisable on the skin of white people, but difficult to see on the
dark skin of the negro. In the course of five or six days the insect, in
consequence of the growth of the numerous eggs, swells up and appears
as a white ball, the size of a small pea, on which the head looks merely
like a small brown spot (see fig. 54). In this manner a small subcu-

FIG. 53.—Sand-flea, female.
After Karsten.
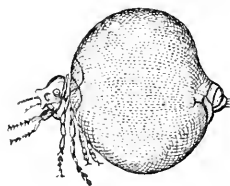
FIG. 54. — Sand-flea,
impregnated ;   female.
After Karsten.

taneous *swelling* is formed over which at first the skin is not reddened,
but becomes inflamed after a few days. In the centre of the swelling a
dark spot is seen which indicates the point of entrance of the insect and
from beneath which is the enlargement due to ova. No development
of larvæ occurs, nor are the eggs deposited whilst the parasite is in
the skin, for the ova do not leave the body until the parent reaches the
soil, sand, or wood (cracks and fissures of wooden structures) when the
larvæ develop.

The disorders caused by the sand flea are generally but trifling. The
pain of the puncture is so slight that it is mostly not even observed.
Later on the affected part itches, but if the parasite is speedily extracted
—an operation in which negro-women are very expert—no further con-
sequences are apt to ensue. Should this not be done, the skin over
the insect suppurates, the symptoms of irritation become more severe,
inflammation and suppuration result, and the parasite is thrown off in
the discharge. Should the wounds originated by the insects become
septic, a common occurrence on account of the habits of the natives, like

other neglected wounds they cause a wearisome suppuration which may extend to the tendon, sheaths and bones, and may set up gangrene, septicæmia, or tetanus.

The part of the body most frequented by the chigger is, as might be supposed from the fact of its living in the ground, the sole of the foot, especially the toes under the tips of the nails and the digito-plantar folds. More rarely, the male genitals, the thigh, and other parts are affected.

The number of parasites infecting a person varies considerably, but over 300 of these insects have been found on one person.

The *treatment* consists in the removal of the parasite. For this purpose a small opening through which the insect had penetrated is enlarged with a needle, a pointed piece of wood, or a small sharp knife, so that the outline of the swollen chigger is laid bare and easily enucleated. The small wound, after having been antiseptically cleaned with sublimate (1 : 1000) is dressed and soon closes. Unsuccessful attempts at extraction in which the impregnated female is torn, are apt to cause more serious symptoms of inflammation. In such cases it is advisable to lay open the track of the sand-flea by an incision, and to clean it out with a strong solution of nitrate of silver or hydrargyri perchloridi, nitric acid or pure carbolic acid.

In regard to the prophylaxis, protection is afforded from being infested by sand-fleas by anointing the feet with oil of cloves, balsam of copaiba, balsam of Peru, or dusting them with insect powder. It is also advisable to examine the feet twice a day in regions where the sand-flea is common.

It is of great importance to destroy the extracted insect, and not throw it carelessly on the ground so that it may contribute to the further spread of the pest with its brood.

In ships, sand from infected districts should not be shipped as ballast ; though soaking the sand with petroleum has been recommended as a prophylactic. This method is not likely to be adopted on account of danger from fire.

A skin parasite called *moukardam* has been reported from Abyssinia, which is perhaps related to or identical with the chigger.

According to Dempwolff,[1] there occurs in New Guinea a skin disease called *Busch-mucker ;* it principally affects Indians in the bush, and consists of small, itching, red papules on the lower limbs. Constant scratching soon transform these into flat, purulent ulcers that only heal after weeks, and which leave pigment spots that persist for years. This complaint is said to be originated by tiny red *mites.* Balsam of Peru is a certain prophylactic for this ailment, and should be rubbed on the lower extremities previous to every journey into the bush. It also is effective therapeutically on the first day.

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7. THE LARVÆ OF FLIES.

The larvæ of various species of flies occurring principally in warm countries acquire pathological importance from the fact that they sometimes develop in human beings and thus originate more or less serious disturbances.   The diseases induced thereby are comprehended under the term *Myiases*, by Hope (from μυῖα, *i.e.*, a fly).   It is the larvæ that principally come under consideration.

(a) Lucilia macellaria, Robineau-Desvoidy.

Synonyms : *Musca macellaria*, Fabricius ; *Lucilia hominivorax*, Coquerel ; *Calliphora infesta*, Philippi ;   *Calliphora anthropophaga*, Conil ;   *Calliphora macellaria*, Jorge ; *Musca anthropophaga ; Compsomyia rubifrons*, Macquart ; *Somomyia montevidensis*, Bigot ; *Screw-worm fly* (America).

The home of this fly, which belongs to the *Muscides* (blue-bottle, flesh-flies), is America, from the Argentine to the south and west of the United States.   In Brazil the ailment caused by this fly is called *bicheiro* (from *bicho*, Portuguese for worm).   It has recently also been observed in Cochin China by Baurac and in Tonquin by Depied.   Probably also the disease known in India as *peenash* belongs to the same category.
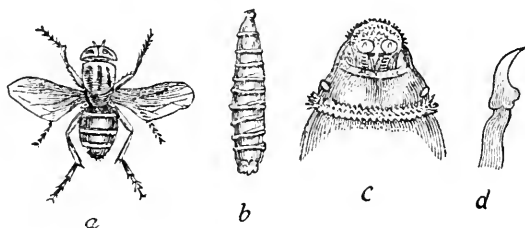
FIG. 55.—*Lucilia macellaria.* After Blanchard.   *a*, Fly ; *b*, larva, natural size ; *c*, anterior part of fly seen from above and much enlarged ; *d*, mouth hook—anterior view, much enlarged.

The *fly* (see fig. 55 *a*) is 9—10 mm. in length, and has a metallic-blue body with thick black hairs, a red forehead, three black longitudinal stripes on the thorax, black legs, and transparent wings quite colourless except at the bases, where they are smoke-coloured.   It deposits its eggs in wounds, ulcers, the nostrils (more particularly if suppuration is present), and in the mouth of man and beast, more especially of persons who are unconscious through sleep, alcohol, &c.   The naso-pharyngeal cavity and the palate are also favourite places.

The larvæ, which develop from the eggs in a few hours (see fig. 55, *b*, *c*, *d*) attain a length of 14—15 mm. ; while alive they are salmon-coloured and when dead opaque-white.   They consist of twelve segments, which carry rows of very small spines, and which are so disposed that they

impart a screw-like appearance to the larva (hence the designation *screw-worm*; they are also provided with two powerful mouth-hooks. The larvæ at once set about their work of destruction, they perforate the mucous membranes (originating severe processes of inflammation), attack the cartilage and deprive the bones of periosteum so that they become carious and necrotic, and are finally cast off through suppuration.

Should the larvæ be situated in the nostril swelling and inflammation of the nose set in accompanied by violent pains and fever; the inflammation may spread more or less over the face and cause an erysipelatous condition; a sanguineous or purulent offensive liquid flows from the nose and, should the worms force their way to the base of the brain, meningitis may set in; and if they eat their way into the orbit or reach it by way of the nasal duct, the eye may be destroyed.

Should the *palate* be attacked dysphagia and dyspnœa may occur.

The larvæ developing in the *ears* bore through the tympanic membrane, disintegrate the middle ear and may even cause meningitis and intra cranial suppuration.

Death not uncommonly ensues through the above-named contingencies or through septicæmia. Of thirty-eight cases compiled by Maillard, twenty-one had a fatal issue.

The *treatment* necessary is the immediate removal of the larvæ by mechanical means, after killing them by injections of chloroform, benzine, oil of turpentine, carbolic acid (2 per cent.), or other antiseptic solutions. Inhalations of chloroform are also recommended. Should the larvæ have penetrated into the frontal sinus or antrum of Highmore, recourse must be had to trephining these cavities.

The *Sarcophila Wohlfahrti*, Portschinsky, which exists in Europe, more particularly in Russia, and originates similar disturbances, is related to the *Lucilia macellaria*.

(b) **Dermatobia noxialis**, Brauer.

Synonyms: *Oestrus Guildingi*, Hope; *Cuterebra noxialis*, Goudot; *Dermatobia cyaniventris*, Macquart.

This fly, which appertains to the family of the *Ostrides* (gad-flies), occurs in America, from Brazil to the south of the United States, where the larva is known by various names. In Mexico it is called *Ver moyocuil* or *mayacuil*, in British Honduras *Cormollote* or *Beef worm* (the fly itself is here called *Anal Coshol*), in Costa Rica it is named *Torcel* and *Suglacuru*, in Columbia it is known as *Nuche* and *Gusano peludo*, in Cayenne it goes under the name of *Vermacaque*, and in Brazil it is designated *Berne* and *Ura*.
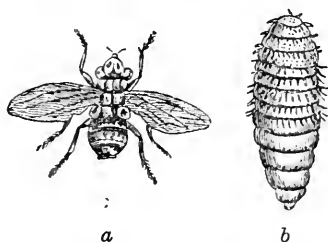
FIG. 56.—*Dermatobia noxialis.* After Goudot. *a*, Fly; *b*, larva.

The *fly* (see fig. 56 *a*) is 14—17 mm. in length. Its head is yellow, the upper surface of the thorax dark grey, the abdomen a bright steel-grey, dirty white at the base, and the wings and legs are of a yellowish-brown colour. It mostly lays its eggs in the skin of cattle, sheep and dogs, and sometimes in the skin of man. The spots preferred by the fly in which to deposit its eggs are, according to Frantzius, the head and trunk, incidentally also the eggs are laid in the conjunctiva and in the lachrymal sac.

The *larvæ* are described variously; the reasons for this being that, according to the stage of their development, they exhibit a different configuration; probably, also, several kinds of dermatobia exist in different countries, as well as in any given district. According to Goudot, the larvæ (see fig. 56 *b*), are 3 cm. long, of a whitish colour, and a club-like shape. They are thicker at the anterior than at the posterior part; the anterior half of the body is beset with hooklets and prickles, and is, besides, provided with two strong oral hooks. They cause an inflammatory reddish swelling, which may become almost the size of a hen's egg (so-called gad-fly boil). A small opening is observed in the centre through which the creature breathes, and through which also it voids its excrement as small black particles mixed with the exuding seropurulent fluid. The posterior extremity is provided with the stigma—the respiratory organs.

Occasionally several larvæ are present in one boil, each one being, nevertheless, separately interred, so that the subcutaneous cellular tissue appears as if honey-combed.

The symptoms consist only of itching and darting pains.

The treatment consists in opening the tumour by means of an incision, and extracting the larva. In Brazil it is customary to trickle tobacco juice into the opening; this causes the larva to protrude somewhat more, and it can then easily be pressed out. The small wound is then treated surgically.

Recently various reports from Africa have been published as to the incidence of gad-fly boils, caused by certain species of flies, which seem to be related to dermatobia noxialis, but the zoology of which has not been determined. F. Plehn reports them from the Tanga Coast; the larvæ observed by him were 5—8 mm. in length, and of a whitish-grey colour.

Nagel, on his own person, made an observation of Myiasis dermatosa œstrosa in Usagara (German East Africa). The larvæ were 2 or 2·5 cm. in length, 6—8 mm. in breadth, of a yellowish-white colour, and exhibited 10—12 segments, armed with hooks.

In British East Africa (on the upper course of the Tana) there exists, according to Kolb, a reddish-brown gad-fly, which he calls *dermatobia Keniæ*, and which the natives call *Ngumba*, an insect capable of flying with incredible swiftness. Persons whilst bathing may have a number of eggs deposited on the skin, and after a week or two nodules, varying in size from a pea to a cherry, form in the skin, especially in the front of the breast; when compressed, a thick white larva, 15 mm. in length and 4 mm. in breadth, may be ejected.

Strachan reports the frequent occurrence of the larvæ of flies in the human skin from Lagos in West Africa. These larvæ seem, by the description, to resemble dermatobia noxialis, but we have no information as to their size.

The gad-fly boils which, according to Arnold and Smith, occur in the Transvaal, Natal, Rhodesia, and on the western shores of the Lake Nyassa, may probably belong to this category. The larvæ are supposed to be deposited by a brown dappled fly, resembling the horse fly; the larger sizes have an average length of 8 mm., and are called *Tsh-izeti* by the natives.

Similar boils with larvæ (usually one, exceptionally several) have, according to Folker, been observed in Guatemala, after the sting of a gnat, called *Gusano sancudo* in that district, and which resembles the common mosquito.

Reports are even forthcoming as to the occurrence of endemic gad-fly boils in high latitudes; Spence mentions this from the Shetland Islands, and Höegh, Thesen and Boeck, from various regions of Norway. In these cases it is probably a question of *Hypoderma bovis*, Latreille.

(c) Ochromyia anthropophaga, Em. Blanchard.

The geographical region of distribution of these flies is Senegambia, especially Cayor, for which reason the larvæ have also been designated *Ver du Cayor*.

The *ochromyia anthropophaga* is a greyish-yellow fly, 8—9 mm. in length.

It is supposed to deposit its eggs in the sand. Thence the larvæ develop, and attacking man and beast as they lie on the sand, penetrate the skin, and rapidly develop. In the skin they generate small inflammatory swellings that become covered with brown scabs. R. Blanchard believes, on the other hand, that the ochromyia anthropophaga, like the dermatobia noxialis, deposits its eggs direct in the skin ; he considers it to be, not a muscide, as Em. Blanchard asserts, but a near relation of the dermatobia and hypodermia.

The *larvæ* are 12 mm. in length, with a breadth of 5 mm. ; they are white in colour, and provided with minute prickly spines.

In six or seven days they again leave their host to be metamorphosed into the pupa stage. The small swellings caused by the larvæ soon heal.

The treatment is the same as in the larvæ of dermatobia noxialis.

In the well-known *Egyptian plague of flies* the species in question were the common house-fly and a few kindred flies.

By preference they attack the places on the face where the skin joins the mucous membrane, the palpebral fissure, the nostrils, and the lips, particularly the angles of the mouth ; these places are apt to be moist, while the skin itself is dry in the warm, dry climate. Inflammation of the conjunctiva, which in Egypt is so prevalent and so severe, is caused by the irritation set up by the flies, and probably also by infective material transmitted by them. The conjunctivitis in question especially affects children, and frequently leads to inflammation and ulceration of the cornea, which in their turn cause cicatricial dimness of vision and even perforation.[1]

The larvæ of flies are also often found in wounds in Egypt. Pruner[2] designates the species *Musca carnaria*. In these cases one often sees the wound covered with black spots which resemble the heads of nails ; these spots exhibit alternate dilatations and contractions, associated with the act of sucking, and when the ulcer is superficial the white body of the parasite can be distinctly seen. These wounds hardly exude any pus but only a sanguineous, watery fluid, and their appearance is bluish and livid.

After the removal of the larvæ by mechanical means the wounds present a honey-combed appearance, and, as may be imagined, are puffy and spongy. Nevertheless, after the removal of the parasites the cavities close with incredible rapidity, and the swellings as rapidly disappear.

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IV.—ORGANIC DISEASES.

TROPICAL APHTHÆ. SPRUE.

DEFINITION.

By the term *tropical aphthæ* is understood a disease that only occurs in warm climates. It is mostly exceedingly chronic, with alternate improvements and aggravations of the condition. It is distinguished by a peculiar affection of the mouth and obstinate diarrhœa, which tend to extreme emaciation and anæmia, and in many cases it has a fatal termination. Some observers, such as Van der Burg and Manson, regard this ailment as a disease *sui generis*, whereas other observers, such as Fayrer, do not differentiate it sharply from the *chronic diarrhœa of tropical countries*.

SYNONYMS.

Aphthæ orientales, Stomatitis intertropica, Aphthœo-gastroenteritis tropica, Aphthoïdes indicæ chronicæ, Gastro-enteritis apthosa indica, Plegmasia membranæ mucosæ gastro-pulmonalis, Psilosis linguæ, Diarrhœa alba ; Tropical Sprue, Indian Sprue, Chronic tropical diarrhœa, Cachectic diarrhœa, White flux, White purging ; Indische Spruw ; Seriawan (Malay).

Probably *Ceylon sore mouth* and the illness known as *hill diarrhœa* and *hill trot*, which occurs on the hills in India in persons coming from the plains, especially during the rainy season and sometimes even becomes epidemic, may be of this character.

GEOGRAPHICAL DISTRIBUTION.

The geographical region of distribution of sprue is fairly large. It has been principally observed in the Antilles, the Malay Archipelago, in India and Further India, in Ceylon and on the coast of South China (Amoy). Personally, I have never seen it in Japan, where, according to Manson, it is said to occur.

The first notification of this disease was furnished by Hillary, who reported on it in his observations made in Barbados in 1776.

ETIOLOGY.

The etiology of sprue is not known. *Climatic influences* certainly play a large part in it, but we are not aware which factor of a tropical climate causes the disease. According to Manson, the course of the disease in Manila and the Straits Settlements is more rapid than in Amoy, which is in a subtropical position.

In 1876, Normand found a small species of nematode (0·7—1 mm. in length and 0·035—0·05 in breadth) in the stools of soldiers with chronic diarrhœa who had returned to Toulon from Cochin China.   At the autopsy he found a larger one (2·2 mm. in length and 0·034 in breadth) in the intestine.   They were termed respectively *anguillula stercoralis* and *anguillula intestinalis* by Bavay and were regarded as the causes of the so-called *Cochin China diarrhœa*, which is identical with the chronic diarrhœa of other countries.   In 1882, however, Leuckart pointed out that the two kinds were two generations of the same species of which one (anguillula intestinalis) is hermaphroditic and lives in the intestine, while its embryos (anguillula stercoralis) escape into the open and there attain puberty and multiply ; their progeny again invade the intestinal canal of man in the shape of filarial-like larvæ.   In the intestine they become the hermaphroditic parent worms.   Leuckart named the parasites *rhabdonema strongyloides*.   As has been demonstrated by Grassi and Leichtenstern, this is not a question of an exclusive *heterogeneity*, but only of a facultative one.   The embryos of the anguillula intestinalis may also be transformed direct into the filaria-like larvæ.

Whichever of these obtain is a matter which, according to Leichtenstern's investigations, is not dependent on conditions of culture or life, such as temperature, moisture, &c., but rests on an inherent quality of the embryos in question.   In the tropical anguillula the heterogeneity, however, seems to predominate, but in the anguillula of temperate climates the direct metamorphosis obtains.   Leichtenstern is of opinion that the anguillula which in its tropical home principally generates the sexual intermediate generation, called *rhabditis stercoralis* by this author, is gradually transformed more and more into an anguillula in the temperate zone, the embryos of which are originally destined for direct larval development ; in the tropics the maintenance of the species is accomplished by means of the progeny of the sexual intermediate generation, whereas in temperate zones the more sensitive generations of rhabditis gradually die off, so that the hardier directly generated larvæ undertake the propagation more and more.

Anguillula-ova only appear in the stools after strong purgatives. Those containing fully developed embryos are found, several together, lying side by side in a delicate tube.

This parasite does not appear to possess any particular pathological importance.   In any case it is not the cause of Cochin China diarrhœa as it was formerly considered to be.   On the one hand it is very often absent in this illness, particularly at its commencement ; on the other hand, it exists in persons who do not suffer from diarrhœa.

Its geographical region of distribution has been demonstrated to be a fairly large one, almost similar to that of ankylostomum duodenale, with which it is often found in company.[1]

The disease never appears epidemically and is certainly not contagious. It occurs principally in *Europeans*, more rarely in natives.   Of 203 cases from the Dutch Indies compiled by Van der Burg, 171 related to Europeans, and 32 to natives.   The disease principally affects Europeans who have lived long in warm climates.   Manson's patients had all been in the East

[1] Hirsch.   Handb. der histor. geogr.   Path. ii., 1883, p. 225.   Braun.   Die tierischen Parasite der Menschen.   2nd edition, 1895, p. 218.

Leichtenstern.   Ueber anguillula intestinalis.   *Deutsche med. Wochenschr.*, 1898, No. 8, p. 118.   Zur Lebensgeschichte der Anguillula intestinalis.   *Cbl. f. Bakt.*, xxv., 1899, No. 6, p. 226.

Pappenheim.   Ein sporadischer Fall von Anguillula intestinalis in Ostpreussen. Ibid., xxvi., 1899, Nos. 20 and 21, p. 608.   M. Braun.   Bemerkungen über denselben. Ibid., p. 612.   W. Zinn.   Ueber Anguillula intestinalis.   Ibid., Nos. 22 and 23, p. 696.

According to the most recent investigations of Askanazy (*Cbl. f. Bakt.*, xxvii., 1900, Nos. 16 and 17, p. 569), the anguillula intestinalis *bores itself into the intestinal wall*, especially the mucous membrane, in order to obtain food and to deposit its ova.   It may therefore incidentally attain the circulation, as Teissier observed (*Arch. de med. expér. et d'anat. path.*, vii., 1895, p. 675) in a patient with diarrhœa and irregular intermittent fever.   The intestinal evacuations of this patient contained anguillula stercoralis and identical worms were found *in the blood*, which disappeared with the fever after three days, so that the author considered the latter was caused by the parasites.

over ten years. Sometimes the disease develops after the return to Europe, occasionally months, or even years elapsing after the patients have left the tropics.

Middle-aged persons seem most prone to contract the ailment, nevertheless, it is also observed in children and old people.

Women are more often attacked than men; pregnancy and lactation appear particularly to have a predisposing effect.

Moreover, according to Van der Burg, weakly persons more frequently than the strong are attacked, the rich more frequently than the poor and civilians more frequently than soldiers.

The following are brought forward as *incidental causes:* exhausting diseases, more particularly of the intestinal canal, such as dysentery and acute enteritis; frequent confinements, miscarriages, menorrhagia, bad food, chills, which so frequently occur in the tropics and cause congestion of the internal organs more particularly of the liver and intestinal tract; irritation of the intestinal canal through partaking of very hot or very cold drinks; eating highly seasoned dishes (Cantlie throws the blame on the sharp vegetable oils which the Chinese and Indian cooks usually use for cooking purposes); and the use of mercurials, especially calomel.

The *abuse of alcohol*, according to Van der Burg, plays no part in the etiology of sprue, whereas Schneider (according to a verbal communication) observed the ailment, especially in hard drinkers, during his thirty years' medical practice in the Dutch Indies. He attributes the circumstance of the disease being at the present time less frequent to the more moderate habits of the Europeans during late years.

SYMPTOMATOLOGY.

The disease commences very insidiously, so that patients are rarely able to accurately state the time of its commencement. The symptoms of *stomachic and intestinal catarrh* always precede the setting in of the mouth affection. The patients complain of fulness, pressure and uneasiness in the region of the stomach, which are aggravated after taking food; they also complain of eructation of gas and pungent, sour or rancid fluid, heartburn and a gnawing pain under the right shoulder-blade, which, however, disappears after the belching up of gas. The appetite is sometimes very large, sometimes it is bad. The stool is irregular : morning diarrhœa alternates with constipation and the intestinal evacuations, at first bilious, are later on pale, clayey and frothy. Occasionally vomiting also sets in, and this often returns daily at exactly the same time, mostly midday, and is generally announced by a feeling of pressure in the forehead and sharp pains in the throat, more particularly the right tonsil (Van der Burg). The vomit is usually very sour and sometimes has a faintish taste, and it contains a great deal of mucus. The epigastrium is distended but is not very painful on pressure.

The *tongue* at first exhibits no abnormalities. When, however, the disease has made further inroads and the symptoms of stomachic and intestinal catarrh increase, *small raised red spots* appear on the tongue, more especially on the edges and tip, and these spots spread gradually over the entire surface of the tongue, which in consequence loses its normal roughness and exhibits a *red, smooth, dry, shiny* appearance *as if varnished.* The epithelium and papillæ appear to have vanished. The tongue in addition becomes narrower and more pointed, and can only with difficulty be extruded, so that when requested to do so the patients can only open the mouth, the tongue not moving.

Very frequently, often before the changes of the tongue, a small ulcer is observed between the two last molar teeth of the upper and lower jaws, sometimes on one sometimes on both sides; this in British India is known as *Crombie's molar ulcer*.

During the further course of the disease shallow transverse fissures form on the surface of the tongue, and small cracks appear on its edges; from time to time also small and very sensitive blisters develop on the edges, tip and frænum, and also on the cheeks and lips; these blebs burst and leave small excoriations.

The tongue is remarkably sensitive, speech is painful and difficult; only the most insipid foods can be eaten; sour, salty or highly seasoned dishes and spirits causing pain. Even mastication is difficult. The sense of taste is altered, occasionally also the sense of smell. A desire for coolness and moisture in the mouth is always present. Sometimes salivation with or without swelling of the parotid sets in. The gums, palate, throat and œsophagus may likewise be reddened, raw and sensitive, so that swallowing becomes painful.

In this stage of the disease *atrophy of the liver* is usually demonstrable by percussion. The urine is diminished, dark and rendered opaque by sediment of urates. Sometimes the urine contains albumen, but no casts (Van der Burg). In women menstruation is generally regular, but profuse; it ceases during the later course of the disease. The skin is dry and the secretion of perspiration almost ceases.

In consequence of the diminished quantity of nourishment taken, and the continuous stomachic and intestinal catarrh, the patients gradually become *emaciated* and *anæmic*. Their power of exertion diminishes more and more, the slightest bodily exertion fatigues them, and their mood is irritable and low spirited, bordering on melancholia.

The illness makes further strides under alternate aggravations and improvements, lasting for months or even years.

The appetite gradually disappears entirely, and vomiting follows whatever is eaten. The stools become thinner, more watery and more profuse and are accompanied by severe flatulence. Their colour mostly resembles that of diluted milk, sometimes it is grey or yellow, the smell is fetid or mouldy, sometimes fishy, with an acid reaction (Thin). The presence of blood in the stools is very rare. The attacks of diarrhœa mostly set in early in the morning and after them the patients, who have now become so weak that they cannot leave their bed, feel exhausted but relieved. During the exacerbations sensitive erosions on the anus and in women on the vulva not uncommonly occur.

The abdomen is distended, the epigastrium very tender on pressure, the liver still more atrophied. It is also possible that a dry cough, with an occasional stitch in the side and difficulty in breathing, may set in. The voice becomes harsh, hoarse, or aphonic. The face appears drawn and wan and exhibits a grey or dirty yellow colour. Brown pigment spots are sometimes found on the skin and the lower extremities are occasionally œdematous; this being more particularly the case in children. Profuse sweats, mostly setting in at night, contribute to the further enfeeblement of the patients. In some cases during the last phases of life slight fever sets in, whereas in other cases the temperature is subnormal. At last, the patients, being in a condition of the most extreme exhaustion, may succumb to intercurrent diseases, or the fatal issue may be caused merely by general failure of strength.

If the illness has not made much advance recovery is possible and is to be expected, especially if the patients return to Europe; it is always,

however, very protracted and relapses frequently set in particularly in such patients as return to the tropics. The liver remains permanently shrunken even when recovery has taken place (Van der Burg).

The *duration* of the disease varies. The course is occasionally sub-acute, lasting one or two years; in other cases it may drag on for ten to fifteen years. A great deal depends on such circumstances as the condition of the patients and the method of treatment adopted.

The typical features of the disease is not always fully developed in tropical aphthæ. Thus diarrhœa may not be present; the stools remaining firm but pale. In some cases, on the other hand, the mouth affection and dyspepsia are not prominent. Sometimes during the course of the disease a change of symptoms occurs, inasmuch as in the earlier stages the mouth affection and dyspepsia predominate, whereas later on the diarrhœa is the prominent symptom. Occasionally the actual symptoms of the disease subside, but digestion and assimilation are permanently impaired in consequence of the atrophy of the intestine. In such cases the emaciation becomes still more extreme, and the patients finally succumb to inanition.

Thin differentiates *three forms* of sprue. In the first form, which is frequent in the Malay Archipelago, the mouth and throat affection develops early and forms the most pronounced and unpleasant symptom. In the second form, which occurs more frequently in British India, the mouth symptoms only set in at a later stage of the disease. The third form is distinguished by its slow course, and is observed in elderly people, or persons who have lived long in the East. To this group belong also those cases which only develop long after the patients have returned to their native land.

PATHOLOGICAL ANATOMY.

The pathological changes which have been observed in persons who have died of sprue are as follows:—

All the organs are distinguished by *extreme anæmia* and more or less general *atrophy*.

The covering of epithelium is lacking on the *tongue* and the papillæ are obliterated.

The mucous membrane of the entire intestinal canal is pale, thin and transparent. In some parts the epithelial covering is lacking. The intestinal villi and Lieberkühn's follicles are atrophic and the solitary glands and Peyer's patches have more or less disappeared. Here and there small round indurations, about the size of a pin's head, and surrounded by a dark pigmented or red area, are met with; they represent small cyst-like dilatations of follicles filled with a grumous purulent material, and occasionally also small abscesses are met with (Manson). Sometimes ulcerations are found in the ileum or colon, or pigmented patches (thin cicatrices) show where an ulcer has healed. Fatty or amyloid degeneration of the intestinal mucous membrane has also been observed. The sub-mucosa in places exhibits cirrhotic changes, especially in the ileum.

The *mesentery, omentum,* and *mesenteric glands* are atrophied, occasionally the last named are enlarged.

The *liver* is small, pale and flabby, occasionally cirrhotic.

The *pancreas, spleen* and *kidneys* are usually found to be atrophied. The pancreas in a case of Drysdale's was extremely cirrhotic; sometimes, also, this organ contains centres of degeneration, and even suppurative foci (Manson).

The *myocardium* is soft and relaxed.

DIAGNOSIS.

The diagnosis of tropical aphthæ presents no difficulties in well-developed cases. It is sufficiently characterised by the peculiar *affection of the mouth, the gastro-intestinal catarrh,* and the *atrophy of the liver.* At the commencement of the illness, if the two first-named symptoms are not present, one may feel doubtful whether it is the disease in question, or an ordinary chronic gastro-intestinal catarrh.

Confusion with other diseases of the mouth, such as catarrhal stomatitis, stomatitis due to mercury, ordinary aphthæ, glossitis dissecans, should hardly occur, so that it is sufficient merely to mention them.

The condition of the mouth caused by *betel chewing,* which is very customary in Asia (in India, South China, and the Malay Peninsula), is easily distinguished from sprue. In this ailment the mucous membrane of the oral cavity, and the saliva are vivid red, the teeth are dyed black, the tongue is clean and shiny, and there are excoriations on the lips, which sometimes extend over the whole mouth. In older persons the tongue finally assumes a dark brown, almost black colour in the centre, while the edges are red and fissured, and their surface raw and dry. Around the vivid red lips the skin of the face appears pale, and ulcers frequently develop at the angles of the mouth.

Betel-chewing originates a " contractile, partly agonising but partly pleasant sensation, which causes hunger and thirst to be ignored, and also involves the nervous system " (Van der Burg). No injurious effect is known to ensue. The mixture (betel) that is chewed, consists of a piece of areca nut, with or without gum, and some tobacco embedded in powdered chalk made from the nacreous layer of the mussel shell, made into a pulp with a little water, and then rolled in a leaf of the betel plant.

PROGNOSIS.

The prognosis of sprue is always serious. Slight cases may recover if the patients submit strictly to the treatment, which is principally dietetic. Should the disease have made further advances, and atrophy of the liver obtains, recovery can only be hoped for if the patients at once seek a cooler climate or return to Europe; but even then many patients succumb. Relapses frequently occur, especially when the patients return to a hot climate. The prognosis is particularly unfavourable in persons over 50 years of age, and those who have been enfeebled by previous malaria.

TREATMENT.

The treatment of sprue is *dietetic,* even when the patients have returned to Europe.

A *pure milk diet* is mostly recommended. One should commence with $1-1\frac{1}{2}$ litres daily, and gradually increase the quantity to $2-3\frac{1}{2}$ litres, which should be taken in small portions every hour; it is best taken with a teaspoon, or through a thin glass tube, or from a baby's bottle. The milk may be taken cold or warm, according as the patient prefers it.

Although physicians so experienced as Fayrer and Roux, recommend that milk be given *newly milked* and *unboiled,* we cannot endorse this advice, on account of the dangers known to accrue from drinking fresh milk. Should it be necessary to dilute the milk, water, lime water or soda water may be added. Buchanan recommends that alkalies be added, (sodii bicarb., potass. bicarb., sodii chlorinatæ, āā 0·3 to $\frac{1}{2}$ litre). Lamb advises that the digestibility of the milk be increased by removing the lime, which according to Wright's prescription, is accomplished by the addition of citrate of soda (1 : 400).

If milk cannot be borne, or if there is an objection to it—Van der Burg quite eschews it—gruels and paps (arrow-root, sago, tapioca, rice water, barley water, oatmeal gruel, maize flour, Nestlé's milk food and similar preparations) should be given.

When the condition has improved by means of the milk cure or farinaceous foods, thin broths, beef tea, meat juice, softly boiled or raw eggs, and scraped raw meat may be tried, and later on also other easily digestible meats (calf's sweetbread, poultry, roast beef, raw scraped ham), toast, stale bread, biscuits, digestible vegetables (spinach, purée of potato, well roasted sweet potatoes, carrots, asparagus), or farinaceous foods may be taken. The greatest care, however, must be taken in the diet, and the stools constantly examined. All acid, salty and seasoned foods are contra-indicated, as also are wines, spirits and coffee. The only drinks allowed besides milk, are cold water and iced water, or weak cold infusions of tea. Cantlie, on the other hand, recommends hot water and rice water (an infusion of roasted rice). Smoking is prohibited.

The carrying out of this *régime* requires great patience and self-denial on the part of the patients, but recovery can only be hoped for if it is carried out systematically and with perseverance. Errors in diet, to which patients seem prone after improvement in the condition has set in, are always immediately followed by relapses, requiring the patients to immediately return to the milk diet. Ordinary diet can only be resumed after the patients have passed normally formed stools for about three months (Roux).

In the Dutch Indies a style of treatment is largely adopted, which, irrational as it appears *à priori*, is supposed to have favourable results even when resorted to in the last stage of the disease, and which Van der Burg and others have found beneficial. This is the *fruit cure*. The following fruits are given to the patients in great quantities, either fresh or preserved, without sugar : strawberries, apricots, peaches, apples, pears, grapes, bananas, mangostenes, cucumbers, melons, pumpkins, and other watery fruits, as well as the juice of oranges and pumeloes. Pine apples and very sour fruits are not allowed. In any case, this cure might be tried as a last resource. The efficacy of the cure is probably due to the acids contained in the fruits.

In British India and Siam the *bael fruit* (*ægle marmelos*, which also grows in Ceylon and Java) is much used in the treatment of intestinal flux, either in a raw state or variously prepared as lemonade, extract, decoction, or syrup. This fruit is distinguished by its copious contents of tannin.

Warmth and *rest* are two remedies which should not be undervalued. The patients should wear a woollen abdominal belt, and in other respects should be warmly clad. They should not be permitted to go out in cold or damp weather. It is advisable to adopt a recumbent position during the first period, and even after an improvement of the condition has set in patients must guard against exertions of all kinds, for fatigue is as liable to cause relapses of the disease as chills.

Däubler recommends washing out the stomach.

A subordinate part is played by *drugs* in the treatment of tropical aphthæ. *Bismuth, alkaline salts*, particularly in the form of Carlsbad water and salts are used, also *digestive fermentatives*, such as pepsine, ingluvin, pancreatin, papain (or fresh papaya fruit), diastase, &c. Van der Burg also recommends *mineral salts*, especially sulphates. Begg highly advocates the use of *santonin* (yellow, therefore impure), which, after giving a dose of castor oil, he administers for six successive days (0·3 in a teaspoonful of olive oil). This method of treatment, however, appears to have found no supporters.

Opium must be resorted to when there is severe abdominal pain and very violent diarrhœa ; great care must be exercised in its administra-

tion.   When there is severe diarrhœa, starch enemata, with the addition of opium may be tried.

Priessnitz's compresses are often found of service in relieving *abdominal pains*, and it is advisable in any case to apply these every night and morning for two hours.

Constipation occasionally necessitates the use of mild aperients, such as castor oil, rhubarb, &c.   Manson advises that the treatment be commenced with an aperient and that no food be given till it has acted.

Powdered vegetable charcoal should be given when there is great *flatulence.*

In Shanghai various mercurial preparations are in use, or *Rein's mixture*, which consists of a decoction of the rinds of simaruba and cinnamon ; along with the mixture carbonate of calcium (powdered cuttle-fish bone or crab's eyes) is given in large doses (two teaspoonfuls at a time), in conjunction with alteratives.   Henderson found the former treatment efficacious in chronic diarrhœa but doubts its usefulness in actual psilosis.   Manson observed a transient improvement, *i.e.*, cessation of the diarrhœa, in one case, but after a few weeks death ensued from exhaustion.

Crombie recommends liquor hydrargyri perchloridi for *hill diarrhœa*, 10 to 15 drops before each meal.

The mouth affection is combated by means of rinsing with carbolic acid 1 per cent. alum, chlorate of potash, common salt, and by touching the ulcers with the sulphate of copper or nitrate of silver pencil. Amelioration is also afforded by smearing the tongue with cacao butter, or other mild grease before eating.   According to Van der Burg, however, the most satisfactory results have been obtained with inunctions of the juice of pterocarpus indicus or rinsings with a tincture made from the rind of this tree.

It is advisable to pencil the tongue with cocaine (1 to 10 per cent.) before meals.

In convalescence the careful use of Amaris and tonics are indicated (wine, quinine, iron, arsenic).

In North America, particularly in the N.W. States, a similar complaint described under the name of *stomatitis materna* or *nursing sore mouth*, occurs in pregnant and nursing women.   It occurs endemically, but is less malignant than sprue and seldom causes death. It is mentioned in Hirsch, iii., p. 169.   In discussing tropical aphthæ Heymann mentions that similar mouth phenomena without diarrhœa are observed during pregnancy, but that at the termination of that period it disappears spontaneously without detriment to mother or child.

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II.

TROPICAL DYSENTERY.

DEFINITION.

Dysentery is an infectious inflammation of the large intestine, which in advanced stages causes destruction of tissue and the formation of ulcers ; the characteristic features of the disease are abdominal pains, tenesmus, and frequent but scanty muco-purulent and bloody stools.

It is a question that is still waiting to be solved, and which cannot be decided until the etiology of the disease is confirmed, whether dysentery is a specific disease or, as is largely assumed, whether it is attributable to a variety of causes ; nor has it been settled whether *tropical dysentery* is etiologically identical with the dysentery of temperate climates.

As dysentery is minutely described in all manuals and text-books, I think it is permissible for me to confine myself to discussing the most important points.

SYNONYMS.

Dysentery, Bloody flux, Ruhr, Dysenterie, Tormina, Difficultas intestinorum, Rheuma s. fluxus ventris, Fluxus cruentus, dysentericus, torminosus, Febris dysenterica.

HISTORY.

Dysentery has been known since the most remote period. Doubtless, however, other affections, such as diarrhœa, typhoid, and other intestinal diseases have often been confounded with it. In Eber's papyrus, which at the very latest, is ascribed to 1550 B.C., there are suggestions of diseases resembling dysentery, and in the ancient Indian writings (Ayur-Veda, &c.) dysentery is mentioned under the name of Atisar. In the writings of Hippocrates (460−377 B.C.) the disease is exhaustively described, and Herodotus (484−407 B.C.) reports on an epidemic which broke out in the Persian army as it marched through Thessaly. There were already excellent delineations of the disease in ancient times, of which that of Aretaeus (40—100 A.D.) deserves special mention. Galen (131—201 A.D.) attributed dysentery to pungent juices which originate from the bile, and this dictum remained as the leading opinion until the seventeenth century. In the latter part of the seventeenth century Sydenham declared dysentery to be a general disease, a fever localised in the intestine. During the next century considerable knowledge respecting the disease was gained. About the middle of the eighteenth century Morgagni (1747) first described the anatomical changes appertaining to dysentery.

The first reports of tropical dysentery date from the seventeenth century and originate from Bontius, who reported the disease from the East Indies in 1642, and Piso, who reported it from the West Indies in 1648.

GEOGRAPHICAL DISTRIBUTION.

Dysentery occurs in *all latitudes*. Sporadic cases are even observed in the coldest inhabited districts, such as Iceland and Greenland ; it therefore oversteps the boundary which is set on malarial diseases, reaching even the highest latitudes. It appears sporadically as well as epidemically in all temperate climates. But as the tropics are approached it generally gains in frequency and severity. It, however, prevails *endemically in tropical* and *subtropical countries only*, so that these regions may be regarded as the home of the disease.

The following places may be regarded as the *principal centres* of dysentery : Asia Minor, Syria, Arabia, India, especially the presidency of Madras, Ceylon, Further India, the Malay Archipelago, particularly Java, the southern and eastern coasts of China especially in Hong Kong, Amoy, Ningpo and Shanghai, Japan, Egypt (the littoral and the delta of the Nile), Algiers, Morocco, the West Coast of Africa, South Africa (more especially Bechuanaland, Transvaal, Natal), East Africa with the East African Islands (Zanzibar, Madagascar, Réunion, Mauritius, the Seychelles), Abyssinia, Soudan and Nubia, a few States of North America (particularly North Carolina, South Carolina, Georgia), Mexico, Central America, the West Indies, a large part of South America (Venezuela, Guiana, Brazil, Paraguay, Argentine, Chili, Peru) and Polynesia (New Caledonia and the Fiji, Mangarewa) and Sandwich Islands.

In Europe the endemic occurrence of the disease is confined to small centres situated in the south ; these are found mostly in Spain, the southern provinces of Italy, Sicily, Greece especially the Pelopennes, Turkey, Bulgaria and Roumania especially the valley of the Danube.

Within this large region of distribution dysentery is not endemic in all parts ; very frequently *certain localities* are visited by the disease, whereas other localities in the vicinity, and presenting similar climatic conditions, remain free. As an instance, Singapore enjoys almost absolute immunity, while in the southern point of the Malay Peninsula close by, the disease is common.

ETIOLOGY.

Dysentery is doubtless of *parasitic origin*, but the micro-organism which originates it is not known for certain. It is questionable if dysentery etiologically represents a specific disease.

It cannot be positively asserted that the disease is caused by any of the various bacilli (Chantemesse and Widal, Ogata, Grigorieff and others), or cocci (Zancarol, Silvestri and others) which are found in dysenteric evacuations or in the tissue of the intestines. Nor can it be said with certainty that certain amœba *(amœba coli* Lösch) or the bacteria of Lösch, Sonsino, Koch, Kartulis, Councilman and Lafleur, &c., which have been found in the dysenteric stools, in the ulcerated intestinal walls, particularly at the base of the ulcer, or in hepatic abscesses associated with dysentery are the real factors in producing the disease. The amœba met with in tropical dysentery are, however, not limited to the tropics, for they have also been demonstrated in North America, Germany, Austria, France, &c.

According to Kartulis, these amœba when at rest are of oval shape and are 12—30 μ in length. A finely granulated endoplasm and a hyaline ectoplasm can be differentiated, and they possess a faintly shining nucleus 5—7 μ in length, which is, however, generally concealed by granules in the plasma, and by foreign bodies that have been taken up, such as red and white blood corpuscles, bacteria, &c. Sometimes these amœba have two or even more nuclei ; sometimes there are as many as ten vacuoles grouped round the nucleus which often appear to harbour small granules.

The demonstration of the amœba is very simple. A particle of mucus is removed from the stool with a platinum wire hook maintained at about the temperature of

the body, and placed on a warm slide. If stained preparations are desired a fresh flake of mucus is fixed with concentrated solution of sublimate, hardened with pure alcohol and then doubly stained with hæmotoxylin and eosin.

In Egypt, Kartulis found amœbæ in all cases of real dysentery (in 150 cases); they were found in the stools, in the walls of the intestines, and also in the pus from dysenteric hepatic abscesses; they were not present in other diseases, and only very seldom in healthy persons.

Kartulis, as well as other observers, succeeded in producing dysenteric-like symptoms in cats (other animals prove unsuitable for this experiment) by injecting the pus of liver abscess into the rectum. On the other hand, no investigator has hitherto succeeded in making a pure culture of the amœbæ, which in themselves contain bacteria on the presence of which their growth appears to depend. Kartulis' observations have been confirmed by Kruse and Pasquale, who also made their observations in Egypt, and who also regard the amœba as the cause of dysentery, at least as far as Egypt is concerned.

The following facts are adduced in opposition to this opinion :—

(1) There are cases of sporadic, epidemic and endemic *dysentery*, even in Egypt, in which *no amœbæ* whatever are present : Arnaud, Zancarol (in Egypt), Celli and Fiocca (in Italy and Egypt), &c. Kruse and Pasquale also found no amœbæ in ten out of fifty cases of dysentery examined, and attributed their absence to the long duration of the disease, previous treatment, &c. Gasser (Algiers) examined 109 cases of acute dysentery and thirty-four cases of chronic dysentery, and demonstrated amœbæ in variable quantities in forty-five (41·3 per cent.) of the acute cases, and in thirteen (38·2 per cent.) of the chronic cases. There seemed to be no relation between the number of amœbæ and the severity of the disease. In two of the fatal cases there were but very few amœbæ, whereas in several mild cases they were very numerous. Their number widely varied in cases that were clinically similar and in which the evacuations were similar. In one fatal case, with extensive ulceration of the bowels, amœbæ could not be discovered either during life or *post mortem.*

(2) Amœbæ are frequently found in the fæces of *healthy persons* who have never had dysentery, and in the evacuations of persons suffering from *other diseases*, particularly diarrhœa (Grassi, Lewis, Cunningham, Calandruccio, Schuberg, Celli and Fiocca, &c.). Gasser examined twenty healthy persons simultaneously with the above-named cases of dysentery, and demonstrated amœbæ in 20 per cent. of them. The amœbæ from healthy persons, according to Schuberg, exhibit no essential difference either in their size or structure from those met with in dysentery (Romer also failed to make out any difference between the amœba of tropical and European dysentery). The fact that dysenteric symptoms can be set up in the cat by the former but not by the latter by no means proves that the tropical amœbæ are pathogenic and the European non-pathogenic, for the experiments were not conducted with pure cultures of amœbæ, but with stools which always contained other micro-organisms as well. Celli and Fiocca were able to induce dysentery in cats by means of evacuations in which the amœbæ had been killed by heating. Zancarol caused dysentery also in cats, with dysenteric stools that contained no amœbæ, with the pus of hepatic abscesses that contained no amœbæ, and with pure cultures of streptococci. Zancarol also produced dysentery in cats without amœbæ by administering dysenteric intestinal evacuations containing amœbæ. Hassler and Boisson likewise produced the disease, without amœbæ, in a dog, by feeding him with pus from a hepatic abscess which contained amœbæ. Kruse, Pasquale, and Kartulis, each induced dysentery in cats by means of hepatic abscess pus which contained no micro-organisms except amœbæ. The experiments, however, are not conclusive, for as Gasser has pointed out, dysentery may be caused by substances having a purely mechanical effect, such as sterilised vegetable soil floated in sterilised water; irritating chemical products of the dead bacteria may also be present in the pus and set up symptoms.

The ætiological influence of amœbæ, therefore, has thus suffered a severe blow through the most recent investigations. Amœbæ may probably be regarded, not as the actual exciting cause, but as the *accompaniment of dysentery*, invading the ulcerated mucous membrane pathologically affected by the primary process of disease. The peculiar frequency with which the amœbæ occur in this disease may perhaps be explained by the circumstance that they find a favourable nutritive soil in the diseased intestine. It is, however, quite probable that their presence contributes to the aggravation of the disease.

Arnaud, Celli and Fiocca, Galli-Valerio and others, consider the *bacterium coli commune* under circumstances still unknown, and it may be other bacteria normally present in the intestine by being transformed into a toxic variety, as possible causes of dysentery. The toxin produced by these micro-organisms, according to Celli, causes the dysenteric infection, while the deep seated disturbances of the tissue are caused by the pyogenous bacteria that are present in the intestine and which congregate in the

damaged mucous membrane. Perhaps Shiga's *bacillus dysentericus* is identical with Celli's *bacterium coli dysentericum*. The former was found by Shiga in Japan in the stools, intestinal walls and mesenteric glands in dysentery. Introduced into the stomach of dogs and cats, Shiga's bacillus originates mucous diarrhœa and gives an agglutinating reaction with the blood-serum of dysenteric patients.

Treille, in several cases of dysentery (Cochin China), found *paramœcium coli*, an organism which has also been observed in intestinal diseases in many countries.

Diseases attended by an intestinal flux resembling true dysentery, but which are attributable to a *mechanical or toxic irritation of the large intestine* through impacted masses of fæces, foreign bodies, worms, decomposed intestinal contents, &c., occasionally occur spasmodically. A dysenteric flux may also be set up by certain *poisons*, especially mercury.

A *continuously high atmospheric* temperature has great influence on the genesis of dysentery, which accounts for its frequent incidence in the *tropics*, and the dependence of the frequency of the disease on the *seasons*. In temperate latitudes, dysentery frequently occurs in the summer and the commencement of the autumn, and it is at these times the epidemics almost always occur. The same condition prevails in the subtropical areas. In Japan I observed dysentery prevailed mostly during the summer months of July, August and September. In Egypt the mortality is greatest during the late summer and autumn (Kartulis). In the tropics, where the temperature is high throughout the year, the disease is most frequent towards the termination of the rainy season, and the commencement of the dry season, *i.e.*, during the periods characterised by striking fluctuations in the temperature, caused by hot days and cold nights. By this variation of temperature chills are caused, which, as we shall see below, play an important part in the etiology of dysentery.

The degree of moisture of the atmosphere and the soil is, according to Hirsch, of subordinate importance in the genesis of dysentery.

The configuration, geological formation and physical character of the *soil* have no influence.

On the other hand, the prevalence of the disease is decidedly influenced by latitude. Reports are to hand from various tropical countries, such as Java, West and East Africa, Cayenne, Jamaica, Martinique, in which as a rule the residents in *mountainous regions* suffer much more from diseases of the intestines, more especially dysentery, than in the valleys near the coast ; this is probably because the liability to take cold is greater at high altitudes.

As dysentery often occurs on *marshy ground* conjointly with malaria, it used formerly to be erroneously considered to be a malarial disease. If the geographical regions of distribution of the two diseases be compared, they will be found to cover both fairly evenly ; in isolated instances, however, they differ considerably from each other. Many points in tropical and subtropical latitudes, which are the most infamous malarial centres on the surface of the globe, are visited *but little or not* at all by dysentery, or very slightly. The peninsula of Gujerat, the islands of Amboina and Grande Terre on Guadeloupe, are instances of this kind. On the other hand, there are severe centres of dysentery in many tropical and subtropical districts that are either quite free from malaria or are but little affected by that disease. Thus dysentery is very prevalent in Oran (Algeria) and Upper Egypt, which are quite free from malaria. The islands of Réunion and Mauritius have from time immemorial had an evil reputation as centres of dysentery, whereas malaria has only appeared there endemically during recent times. Basse-Terre on Guadeloupe, in contradistinction to Grande-Terre, is free from malaria, but liable to dysentery

One point that Hirsch draws particular attention to is that moist soil indirectly predisposes to dysentery on account of its effect on the temperature, more especially as regards its marked daily changes.

In one particular malaria has something in common with dysentery, namely, that both diseases are more frequently observed in *country districts* than in towns.

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Dysentery is not *communicable* from person to person, but the *intestinal evacuations*, in which doubtless the infective matter is contained (the lavatories, night-commodes, enemata, &c.), can convey the disease. In this way the disease can be carried from one place to another.

The virus of disease is introduced into the system, either by the mouth or by being conveyed direct to the mucous membrane of the *rectum*.

In most cases infection takes place through imbibing *water contaminated* by fæcal matter. In Java between 1869 and 1878 the mortality from dysentery amongst the European soldiers of the Dutch-Indian army averaged 13 : 1,000. In 1875 the first artesian well was sunk, and others soon followed. From 1879 to 1883 the mortality from dysentery dropped to 4·2 : 1,000, and at last from 1884 to 1888 it fell to 0·7 : 1,000 (Stokvis).

In garrisoned places which have been provided with wholesome drinking water for ten years past, the illness may be said to have disappeared entirely. The disease has also decreased considerably in the British and French Colonies in consequence of the improvement of the water supplies.

The virus of disease may also be carried by means of *table utensils* or *raw fruits* which have been *contaminated* by the hands of coloured servants suffering from mild or chronic forms of dysentery.

The *period of incubation* given is from three to eight days. Should infection take place *per rectum*, it averages only twenty-four hours, or but little more, as was demonstrated in the cases observed by Lemoine, in which the contagion was caused by the use of a common night-stool by the dysenteric and other persons.

Racial difference plays no part in the etiology of dysentery. Though coloured people are attacked more frequently than the whites, the circumstance is attributable to the unfavourable hygienic conditions under which the former live.

In white people the predisposition to the disease increases after a stay of some years in the tropics.

Neither *sex* nor *age* afford exemption from the disease. Children are more liable to the disease than adults.

As regards *occupation* Davidson asserts that agriculturists are attacked more frequently than persons whose calling is carried on indoors. According to Zancarol, persons who labour in the heat, such as stokers, cooks, or mechanics are particularly predisposed to the disease. Perhaps in the case of stokers and cooks the liability to catch cold no doubt acts as a determining cause.

Chills are above all to be mentioned as predisposing causes, as also the eating of rotten and indigestible articles of food, unripe fruits, insufficient or superabundant nutriment, abuse of alcohol—inebriates usually have severe attacks—impacted masses of fæces, disorders of digestion, hæmorrhoids, pregnancy, excessive venery, enfeeblement through previous diseases, especially malaria, scrofula and typhoid.

Finally, *unfavourable hygienic conditions*, such as uncleanly, damp dwellings, the crowding together of many persons in small, badly-ventilated apartments, foul privies, contamination of the soil and drinking water by quantities of fæces, &c., play an important part, and the epidemic appearance of the disease is often attributable to several of these causes conjointly with such conditions as overwhelming heat, long-lasting drought, &c. Such epidemics are therefore particularly liable to occur

during *war*, and as an accompaniment to *famine*. In almost every long campaign or siege, the outbreak of an epidemic of dysentery amongst the combatants, amongst the besiegers as well as amongst the besieged, is a common occurrence. In rare cases the epidemics assume the character of *pandemics*, which usually extend over several years.

Dysentery often forms the terminal disease in chronic invalids, such as malarial cachectics, tubercular invalids, lepers. It also occurs in prisons, and the mentally afflicted in *asylums*. When dysentery breaks out in jails or asylums it is in all probability due to the insanitary hygienic conditions of the institution.

Recovery from dysentery is no protection from repeated attacks ; on the contrary, the tendency to contract dysentery is increased by the fact of once having had the disease.

PATHOLOGICAL ANATOMY.

According to Virchow two forms of dysentery are differentiated : (1) The *catarrhal*, and (2) the *diphtheric*.

In the catarrhal form the mucosa and submucosa of the intestine are hyperæmic and infiltrated by a sero-purulent exudation. When the inflammation attains a higher degree the purulent exudation in places becomes so thick that the tissue breaks down, and ulceration sets in as a consequence.

In the diphtheric form, according to the less recent views, the exudation consists of amorphous fibrin that has coagulated between the tissue elements and induced necrosis, or as Weigert has taught us, the tissues in consequence of the intensity of the inflammation have become disintegrated and necrosed with the formation of a material similar to coagulated fibrin. The dead tissues are then shed, and more or less extensive ulcerations are left.

The two forms are, however, not sharply differentiated, for there occurs in both different degrees of the same process of inflammation, so that all transitions, from the slightest to the severest degree, are found side by side. This observation holds good for the dysentery of temperate climates as well as for tropical dysentery.

The *large intestine* is mostly the *seat* of the disease, being often affected from the anus to the cæcum. Occasionally also the lower part of the ilium is attacked, but always to a less degree. In very rare cases the process extends still higher. The point of departure of the diseased process is mostly formed either by the cæcum or by the rectum. As Virchow first pointed out the flexures (hepatic, spleen and sigmoid) exhibit the most developed stages of disease, that is places where masses of fæces generally remain the longest, and therefore are wont to irritate the inflammed mucous membrane most.

As to the anatomical changes exhibited by the dysenteric intestine in a mild case or at an early stage of the disease, the mucous membrane assumes a dark or light red hue covered with a layer of hyaline mucus streaked with red here and there. The redness is sometimes diffuse and even, or it becomes most marked at the edges of the prominent folds. In addition punctiform and larger ecchymoses are frequently found, and the mucosa is loosened, friable and easily scraped off with a knife. The solitary follicles frequently appear as swollen greyish-white points, varying in size from a hemp seed to a pea, and surrounded by a congested area. The sub-mucosa also is hyperæmic, permeated by small hæmorrhages

and œdematous. If at this stage of the disease recovery ensues, no cica-trices are left, but a diffuse—more rarely punctiform, slatey pigmentation remains.

At more advanced stages of the disease more or less numerous diseased patches are seen on the hyperæmic and swollen mucous membrane, vary-ing in size from a few millimetres to several centimetres. The patches are at first not deeply coloured and have no gloss, but later they become deeply discoloured or blackish ; here and there they appear as if covered with a grey slough. When these sloughs are shed *ulcers* are left, the size and form of which vary considerably. The depth also varies ; sometimes the ulcers only extend to the mucosa, sometimes they penetrate the sub-mucosa, the muscular coat, and even the serous membrane, so that perforation of the intestinal wall may ensue.

Besides these ulcerations due to superficial or deeply situated necrosis, other ulcers, the size of a pin's head, or a little larger, are met with ; these are distinguished by their round form and sharp edges, and are caused by *solitary follicles*, which have suppurated and necrosed.

A *submucous suppuration* usually appears conjointly with the ulcerative process ; this undermines the mucous membrane and in chronic cases occasionally leads to inflammation of the cellular tissues in the vicinity of the intestine.

In the most severe form of the dysenteric process, in so-called *gangrenous dysentery*, the mucous membrane becomes extensively disinte-grated and is occasionally shed in large, gangrenous patches, or even in the form of long cylindrical masses. Occasionally the large intestine forms a continuous ulcerative surface, from which only here and there small islands of intact mucous membrane protrude.

If the ulceration is not too extensive, the bowel may *heal*. In that case granulation tissue forms in the base of the ulcer ; copious quantities of pus are exuded, and finally a formation of flat, shiny scars takes place. There is, however, no regeneration of the glandular tissue that has perished.

When the ulcers are large, the process of healing, as may be imagined, proceeds very slowly and in consequence the disease assumes a chronic course (*chronic dysentery*).

In chronic dysentery, instead of the hyperæmia that was present formerly, the mucous membrane is found to be pale or slate-coloured ; it is thickened in the vicinity of the ulcers, and the solitary glands are atrophied. The lumen of the large intestine is usually shrunken and its wall sometimes attenuated and sometimes thickened and lardaceous. The gut is frequently attached to neighbouring organs by inflammatory adhesions. The cicatrices originate strictures in consequence of their contraction, especially if they be ring-shaped, and above the strictures gradual dilatation of the intestinal canal and hypertrophy of the muscular coat develop. The mucous membrane of the small intestine, the loops of which may be adherent to one another, is often pale or slate-coloured and the lymphoid constituents, as also Lieberkühn's follicles, appear atrophied.

In " *amœbic dysentery* " the process of disease according to Councilman and Lafleur —whose opinion is shared by Kruse and Pasquale—commences in the *sub-mucosa*. In the sub-mucous tissue invaded by the amœbæ, small infiltrations are formed. These slough and lead to the formation of areas containing a jelly-like pus. The mucous membrane is only involved secondarily in the process and to a less degree, so that typical ulcers with undermined edges ensue. The mucous membrane at the same time is catarrhal and exudes a great deal of mucus.

According to Kelsch also, the sub-mucosa is the chief seat of the inflammation. The

vessels leading to the mucous membrane are involved in the cellular infiltration which invades the sub-mucosa, leading to necrosis with consecutive ulceration in the mucous membrane.

As to *affections of other organs* in consequence of dysentery, it must first be mentioned that the *mesenteric glands* as a rule are hyperæmic and swollen, and become pigmented in later stages or permeated by pus, or present caseous foci.

The *liver* may be of normal size or it may become enlarged and hyperæmic and the seat of simple or multiple abscesses. In chronic dysentery the liver is often in a state of fatty degeneration and in other cases it appears atrophied or cirrhosed.

In the *spleen*, embolisms, areas of softening, and even abscesses are met with.

The *kidneys* in chronic cases often show inflammation of the parenchyma, or more or less atrophy.

In protracted cases *metastatic inflammations*, such as purulent parotitis, pericarditis, pleursy, gangrenous erysipelas thrombosis of the veins with suppurative disintegration, gangrene and noma are met with.

SYMPTOMATOLOGY.

Three forms of dysentery are differentiated clinically : (1) the *catarrhal ;* (2) the *gangrenous ;* and (3) *chronic* form.

1. Catarrhal Dysentery.

Diarrhœa, it may be of a choleraic type and accompanied by general indisposition, may precede an onset of catarrhal dysentery. In the mildest abortive form the disease may not go beyond the stage of these prodromal symptoms.

In other cases the onset of the disease is sudden. *Abdominal pains,* situated mostly in the umbilical region, set in generally at night or early in the morning, and *tenesmus* and the *typical intestinal evacuations* accompany the attack.

The motions to commence with are fæculent ; soon, however, the fæculent character disappears, and only small quantities, rarely more than a tablespoonful, of slimy mucus tinged or streaked with blood is passed. The stools have a peculiar stale odour and mostly exhibit an alkaline, rarely a neutral or acid, reaction (Eichhorst). The motions become still more frequent, and the abdominal pains and tenesmus increase in intensity. In the milder cases the number of stools in the twenty-four hours averages ten to twenty, in serious cases fifty to sixty in twenty-four hours. Sometimes small quantities of pure blood are passed.

After the disease has lasted several days, the character of the stools is apt to change, appearing as a yellowish or reddish fluid in which yellow or red soft little pieces, resembling chopped muscular tissue, float. These particles are cast-off shreds of mucous membrane, or when examined microscopically are found to be composed principally of red blood corpuscles, pus, and intestinal refuse embedded in a viscid slimy material (Heubner.)

In amœbic dysentery Charcot-Leyden's crystals are sometimes found in the stools (Kartulis, Councilman and Lafleur, Römer).

The frequent evacuations cause irritation or actual inflammation of the anus, which in consequence becomes the seat of burning pains.

Sometimes prolapse of the rectum occurs, or tenesmus of the neck of the bladder, with consequent dysuria and strangury.

The abdomen is but rarely distended; in severe cases it is painful on pressure, particularly in the right or left iliac regions. Pruner and Heubner have directed attention to the peculiar resistance, similar to that of an india-rubber tube with fairly thick walls, assumed by the intestines in the diseased portions.

In Cameroon A. Plehn observed pronounced symptoms of *typhlitis* in the majority of Europeans suffering from dysentery, even in the early stages, in which deep-seated ulcerations could hardly have set in; accompanying the typhlitis, Plehn describes considerable exudation into the abdominal cavity. This symptom, however, had no distinctive bearing, for in cases of medium severity it rapidly disappeared under suitable treatment.

The tongue is covered by a white coating. There is generally loss of appetite and intense thirst; vomiting is not frequent. In some cases the patients exhibit slight jaundice. The urine is scanty and concentrated; it is usually free from albumen; the chlorides are diminished.

The fever accompanying the disease is, as a rule, not high, or may be entirely absent. Nevertheless, the patients' strength rapidly decreases.

If correctly treated the disease rarely lasts longer than a week. In some cases, however, it is prolonged over several weeks.

2. Gangrenous Dysentery.

Gangrenous dysentery is either an outcome of the catarrhal form, or commences insidiously as fæculent diarrhœa, accompanied by slight abdominal pain and tenesmus. After a few days mucus and blood appear in the stools, and the abdominal pain and tenesmus become more and more severe. The stools consist of a brownish-red or blackish slimy fluid, with a cadaverous odour, and in which small or large pieces of gangrenous intestinal wall are contained. Sometimes even cylindrical masses a foot long are evacuated. In most of the cases, according to Heubner, however, these do not consist of the intestinal wall itself, but only of mucus. The intestinal evacuations are remarkably frequent, the number averaging 150 to 200 in the twenty-four hours, so that the patients are literally unable to rise from the commode. Sometimes large quantities of pure blood are passed, and death may even ensue from hæmorrhage. Fayrer has pointed out that occasionally the stools are pulpy, and appear to contain neither mucus nor blood; they, however, give off a horribly fetid smell. The prognosis in such cases is bad.

There is in addition great weakness, the pulse is small and frequent, the skin cold and moist, the temperature usually subnormal.

Before death stools are passed involuntarily, so that on approaching the patient's bed a sickly cadaverous odour is experienced.

Sometimes, as in cholera, *algide symptoms*, such as copious stools, anuria, muscular cramps, hoarse voice, singultus, and precordial agony precede the fatal issue.

In other cases in which septicæmia is a concomitant of the dysentery, *typhoid symptoms* set in. The temperature rises, sometimes after an initial rigor or with repeated fits of shivering, and assumes a continued or remittent type. The tongue becomes dry, the mouth foul, and the breath fetid. Cerebral symptoms set in, at first in the form of restlessness and persistent dreams, but later on delirium and stupor supervene. These symptoms may be accompanied by peritonitis or purulent paro-

titis, carbuncles, putrid abscesses in the vicinity of the anus, decubitus, gangrenous erysipelas, &c., the patients mostly dying of extreme prostration.

Death, which generally occurs in the second week of disease, or even later, is mostly due to exhaustion; more rarely it is due to pyæmic or septicæmic infections, intestinal hæmorrhages, perforation of the bowel, peritonitis, or other complications. In many cases the fatal issue occurs rapidly after even a few days' illness.

3. Chronic Dysentery.

Chronic dysentery is for the most part a sequel of the acute form and tropical dysentery has the tendency to become chronic in a far greater degree than either sporadic or epidemic dysentery. After actual or only apparent recovery from acute dysentery relapses may occur and these, after frequent repetitions, assume a continuous or chronic form. In other cases the disease begins insidiously in the form of intermittent diarrhœa. After a longer or shorter period slime and blood are observed in the stools during the exacerbations and some colic and tenesmus are experienced.

The intestinal evacuations in chronic dysentery may vary considerably at different times in the same patient as well as in different persons. As a rule the motions are frequent, five to six daily, or they may not exceed two or three in number; they are thin, sometimes quite watery, of various tints and often give off a foul, repugnant odour, and contain mucus, blood and pus, in various combinations. Occasionally small pieces resembling frog-spawn or sago are present in the motion; these consist partly of exudations from follicular ulcerations, partly of starchy particles, a fact that Virchow was the first to point out. Occasionally blood is so intermixed in the stools that they assume an even brownish-red or blackish-red colour. Firmer masses of fæces and undigested ingredients of food (lienetry) are frequently found in the stools. Pain and tenesmus are but slight or may be entirely absent. Occasionally diarrhœa alternates with constipation and the stools may continue to even assume a normal condition for a short time.

The appetite is sometimes bad, sometimes on the contrary very large, and frequently alternating. The tongue is red and smooth, and deprived of its epithelium, the abdomen is sometimes distended with wind and sometimes flattened; there may or may not be vomiting. Bronchial catarrh has occasionally been noted (Kartulis).

If untreated the disease may drag on for months and years, the patients becoming more and more emaciated and anæmic.

Sometimes hæmorrhages set in, especially in the skin and from the nose. Finally profuse night sweats, œdema and bed sores develop, and the patients die from general exhaustion or succumb to a complication such as pneumonia, Bright's disease, or perforating peritonitis.

Should the ulcers heal, *stricture of the bowel* with consequent intestinal disorders often remain.

The " *amœbic dysentery* " of Councilman and Lafleur is distinguished by a tendency to a chronic course, interrupted by exacerbations and remissions.

The most frequent *complications* observed are *inflammatory symptoms* affecting the liver. These may accompany dysentery, follow it, or even precede it and are indicated by nausea, bilious vomiting, yellow and green stools or motions without bile, heaviness, tension and dull pains in the right hypochondrium, pains in the right shoulder, enlargement of the

liver, and sometimes icterus. These disorders may again disappear or may lead to the formation of *hepatic abscesses* (see the next chapter). Hirsch compiled the histories of 2,377 cases of dysentery with a fatal issue, of which 19·2 per cent. exhibited hepatic abscesses. The frequency of hepatic abscesses associated with dysentery varies in different countries; they are observed most frequently in Egypt and the East Indies.

More rarely *abscess* of the *lung*, of the *brain*, and of the *spleen* occur in connection with dysentery. Scurvy may arise as a complication, more especially in the tropics, but it also appears in temperate latitudes under the unfavourable hygienic conditions which obtain at times in camps, hospitals, prisons, &c. Besides the characteristic affection of the mouth, hæmorrhages in the skin, stools of pure blood and sometimes even vomiting of blood are observed.

During the course of dysentery, or perhaps during convalescence, and more frequently in milder than in the severe cases, *arthritis* with or without effusion occurs. The affection of the joint resembles closely the condition met with in articular rheumatism, and is probably due to a secondary infection with pus cocci. As a rule more than one joint is affected and occasionally even a great many. The ankle and knee-joints are most frequently attacked. This complication usually drags on for months and in exceptional cases leads to anchylosis or suppuration of the joint. Cardiac complications are rarely observed in post-dysenteric arthritic ailments.

Occasionally *intussusception of the intestine* is observed in dysentery. This is recognised by the lack of any fæcal constituents in the stools, attended by vomiting at first bilious and then fæculent, flatulence and collapse.

During the course of convalescence *relapses* occasioned by errors in diet, chills, &c., are frequently observed, especially in patients who have been weakened by previous disease, by the abuse of alcohol, or by too long a stay in the tropics. Generally after recovery from dysentery the intestine remains permanently irritable and inclined to diarrhœa.

Finally, it may be mentioned that in rare cases, *paralysis*, the consequence of more or less extensive inflammation of the peripheral nerves, occurs in dysentery as well as in other infectious diseases, especially diphtheria. Beri-beri even, as we have observed, may become a complication of dysentery. H. Lenhartz, in one case, observed *ataxia* and *aphasia* in intimate conjunction with the disease, and ascribed the cause to an inflammatory process extending to the brain, the medulla oblongata and to the spinal cord. The *percentage of mortality* in dysentery varies according to place and period. Improved hygienic conditions and better treatment has, in general, lessened the mortality during recent years. In Egypt, during Griesinger's time, the mortality averaged from 36 to 40 per cent., whereas Kartulis at the present time computes it at only 2 or 3 per cent. among the Europeans treated. In India the mortality amongst Europeans is given as varying between 3 and 22 per cent., and in natives at 37·5 per cent. In Japan, the mortality observed by me was 7 per cent., while Ogata computed the mortality in Japan to average 24 per cent. (1884-1890).

According to Roux, from 40 to 70 per cent. of persons suffering from chronic dysentery succumb to the disease.

DIAGNOSIS.

In most cases the diagnosis of dysentery offers no particular difficulties; one should, however, never neglect to inspect the evacuations. Dysentery

has to be diagnosed from the lesions which occur in such ailments as catarrh of the large intestine, proctitis, hæmorrhoids, rectal polypi, syphilitic processes and carcinoma of the rectum (examination of the anus and rectum), intussusception of the intestine (especially in children), bilharzial disease (hæmaturia, proof of ova in the stools).

The differentiation between *chronic dysentery* and *chronic diarrhœa* is, however, occasionally more difficult. In the differential diagnosis, the history of disease (acute dysentery having preceded), the presence of tenesmus and the condition of the stools must be taken into account; mucus is rarely absent from the stools, and blood and pus are found at times.

Bertrand and Fontan *identify chronic dysentery with chronic diarrhœa.* The symptoms and pathological-anatomical changes in both diseases, according to these observers, are the same. In chronic diarrhœa, mucus and blood are occasionally found in the stools, and ulcerations of the intestine are met with *post mortem.* If the affection starts in the small intestine the illness commences with diarrhœa, whereas if it originates in the large intestine dysenteric symptoms are present from the commencement. If during the course of the disease the process advances from one part of the bowel to the other, mixed symptoms of entero-colitis develop, under which term Bertrand and Fontan describe both diseases. These authors do not regard tropical aphthæ (sprue) as a specific disease, but are of opinion that the characteristic mouth affection found in sprue, may be present or absent in chronic entero-colitis and may also occur in other chronic ailments such as tuberculosis.

According to Kaufmann, the *pilgrims' diarrhœa,* which frequently breaks out amongst the pilgrims returning from Mecca—usually at the quarantine station of El Tor on the Red Sea—comprises two different intestinal diseases which the author classes as (1) chronic diarrhœa, and (2) a peculiar disease of the large intestine requiring further investigation. Imported cases also appear in Egypt. Kaufmann, in two such cases, found at the autopsy that the entire length of the large intestine was in a state of inflammation. The mucous membrane was loosened, the glands were swollen and irregular, small, slightly raised red points were apparent everywhere, and between these there were greyish-yellow mucous masses (not of a diphtheric nature). These masses contained, microscopically, red blood corpuscles, epithelial cells, bacteria, &c.

PROGNOSIS.

The prognosis of dysentery depends upon the *age* and *constitution* of the patients, and on the *form* of the disease.

Sucklings, old people, persons enfeebled by previous illnesses, and inebriates, are particularly endangered. Pregnant women attacked by dysentery will, according to Van der Burg, probably miscarry and always suffer severely after the expulsion of the fœtus.

As to the different forms of the disease the prognosis is favourable in the *catarrhal form,* death seldom occurring in this variety. On the other hand, the prognosis of *gangrenous dysentery* is in general unfavourable, more especially if large and numerous pieces of cast-off intestinal wall are contained in the stools. Severe hæmorrhages, violent vomiting, paralysis of the sphincter ani, foul tongue, thrush, great uneasiness, delirium, convulsions (in children), hiccough, precordial agony, collapse, algide symptoms and metastases are all to be regarded as *very unfavourable signs.* In *chronic dysentery* the prognosis is decided by the duration of the disease, the severity of the symptoms and the general condition of the patients.

PROPHYLAXIS.

General prophylaxis demands careful attention to general hygiene and the personal avoidance of the above-mentioned incidental causes.

The circumstance that dysentery does not now appear in the tropics with the frequency and severity of thirty to fifty years ago, is to be ascribed to the improvement in the hygienic conditions, especially in regard to water supply, that has taken place during recent years, and to the more rational methods of treatment practised by the doctors of the present day.

In order to avoid the disease spreading, the intestinal evacuations, in which doubtless the infective material is contained, should be *disinfected*, as should also night commodes, utensils, privies, &c., as well as the soiled body and bed linen used by the sick.

In indigestion the use of mild aperients is recommended. Zancarol advises that cold baths should be taken prophylactically throughout the entire year.

TREATMENT.

The principal drugs used in the treatment of dysentery are *calomel* and *ipecacuanha*, the effect of which does not depend solely upon their aperient and emetic qualities. These drugs must be regarded as having a *specific* effect, a fact that does not seem as yet to have been fully acknowledged, at least as far as the German text-books are concerned.

Calomel, which was introduced by Annesley in the treatment of dysentery, and is especially used by the French in Algiers, is used in various ways, sometimes in small frequently repeated doses, sometimes in larger doses taken more rarely. I made use of the latter method and can recommend it warmly as the result of my experience in Japan. I administered calomel in doses of 0·3 to 0·5 every four to six hours ; and if constipation occurred meantime one or two tablespoonfuls of castor oil were administered. On an average a total of 3·0 to 4·0 calomel sufficed to effect a cure. The largest quantity that was ever necessary was 9·0. It was well borne throughout the disease, and never caused the development of stomatitis.

When larger doses of calomel were necessary, mouth troubles were avoided by thoroughly cleaning the teeth, and rinsing the mouth with chlorate of potash.

Kartulis favours the administration of frequently repeated small doses. He prescribes 0·05 to be taken ten or twelve times in twenty-four hours for several days. In subacute and chronic cases he gives even smaller doses. Recently, he gave naphthalin in conjunction with calomel, his prescription being as follows : Calomel 0·5, naphthalini 1·0, ol. bergamott. gtt. iii. F. dos. No. x. ad caps. amyl. S. One capsule every hour.

In *gangrenous dysentery*, according to Dr. Manson and A. Davidson, calomel is *contra-indicated*.

Ipecacuanha, which in 1648 was brought by Piso to Europe from Brazil, where it had been used in the treatment of dysentery, has been principally used in India. According to Fayrer the mortality of the British army, which was 11 per cent. before its use, fell to 5 per cent. after its introduction. The method of administering ipecacuanha adopted in India is in most essentials that recommended by Dock in 1858. If constipation is present a dose of castor oil or some other mild aperient is first given, and then 1·0 to 4·0 ipecacuanha as a bolus in pill-form, or in cachets, or in a little warm water. In order to avoid vomiting being set up, a mustard poultice, a mustard leaf, or a piece of blotting paper sprinkled with oil of mustard is applied to the region of the stomach, and twenty to thirty drops of tincture of opium, or a hypodermic injection

of morphia is given half an hour before the dose of ipecacuanha. The patients must lie still in a horizontal position and take no food or drink for three or four hours. If, notwithstanding these precautions, there should be a tendency to vomit, this must be combated by giving little pieces of ice to suck. If vomiting sets in soon after the administration of the ipecacuanha, a second dose should be given. In mild cases the dose is repeated morning and evening, in severe cases every eight hours, and the treatment is continued until the abdominal pain and tenesmus have disappeared and the stools have become fæculent. In the mildest cases one or two doses are sufficient to effect a cure ; in serious cases the treatment must be continued for several days.

In the gangrenous form, ipecacuanha should be tried first of all.

McDowall recommends that ipecacuanha be always given in the *evening* before going to sleep, never in the morning or during the course of the day.

The *Brazilian* method of administering ipecacuanha, according to Charlopin, is as follows : 4·0 to 8·0 of the root is infused with 150 0 water, and macerated for twelve hours. This infusion is administered once or several times on the first day. On the second day a new infusion is prepared with the root that has already been used, and is given in larger or smaller doses, according to the tolerance of the patient ; the same proceeding is gone through on the third day. Under some circumstances the addition of an aromatic drug or of a little opium is permitted.

Zancarol administers 0·5 ipecacuanha with 0·05 opium, morning and evening, until the tenesmus and blood have disappeared from the stools, this being usually on the fourth and fifth day. Should dysenteric intestinal evacuations reappear, an aperient is administered.

As the usefulness of ipecacuanha is frequently frustrated by its emetic properties (caused by the alkaloid emetin contained therein), preparations liberated from this element have been produced ; of these preparations *radix ipecacuanhæ sine emetina* (Merck) has proved most useful (Kanthack and Caddy).

Opinions differ as to which of these drugs merits the preference. 1 personally prefer *calomel*. According to my experience, when it proved useless, ipecacuanha was also given without results. Though calomel and ipecacuanha have a positive effect in catarrhal dysentery, they have but little effect in the gangrenous form, and according to my opinion the same is the case in chronic dysentery. Roux, in chronic dysentery, has observed favourable results in cases, not too far advanced, from a combination of ipecacuanha, calomel and opium, in the form of Segond's pills. The formula is as follows : Rad. ipecacuanha 0·4, calomel 0·2, extracti opii. 0·05, syr. rhamni catharticæ q. s. ut. f. pil. No. vi. s. : to be taken in twenty-four hours. These are taken for three days, there is then an interval of three or four days, when they are again taken for three days, and so on.

The following are some other remedies used in dysentery :—

Castor oil, which has already been mentioned, of which two to four tablespoonfuls per diem are given during the first days of disease, and later it may be repeated. Hillier also recommends it in chronic dysentery in smaller doses in conjunction with tincture of opium, the dose being 4·0 to 8 0 castor oil, to 4 to 10 drops of tincture of opium, three times a day.

Saline aperients, especially sulphate of soda and sulphate of magnesia, for which French doctors have a special predilection. Magnesium sulphate has also recently gained great renown in India, and the British doctors even prefer it to ipecacuanha. Magnesium sulphate (Epsom salts) is used in a saturated solution, of which even in chronic dysentery, 4 0 to 8·0, with a few drops of diluted sulphuric acid, is given every one or two hours. Buchanan's prescription is as follows : Magnes. sulp. 60 0, acid. sulp. dil. 12·0, tinct. zingib. 12·0, aq. ad 240·0 ; this is continued for two

or three days after the mucus and blood have disappeared from the stools, and it is recommenced if the stools again become dysenteric. If there is constipation in chronic dysentery, castor oil or Carlsbad salts or Carlsbad water are the most suitable aperients.

After convalescence from dysentery it is advisable to take Carlsbad water as an after treatment for a few weeks.

Ailanthus glandulosa (Simaruba) and *cortex radicis granati*, which are usually given together, have been recently recommended by Gelpke and Gräser in the following form : Cort. rad. granat., simarub. āā 10·0, macerated with vin. gall. 750·0 per horas. xx. s: adults six to eight tablespoonfuls, children and infants six to eight teaspoonfuls daily. In Kartulis' experience these drugs are ineffective in the acute stage of the disease, but may do good service in chronic dysentery.

Fructus myrobalani, which is much used in Egypt, and forms one of the ingredients in Schwarz-Lademann's *antidysentricum,* was only found efficient in recent and mild cases by Becker (German East Africa) ; the efficacy, however, that he speaks of is quite as likely to be due to the previous administration of castor oil for three or four days which Schwarz advises.

Ixora dandraca and *hedysarum* are drugs in use in India for dysentery.

Tuphmulunga is an Indian seed soaked in water, the decoction from which, drunk *ad libitum,* is recommended by Fink.

Monsonia ovata is a South African plant which Maberly has used in the form of tincture and has found efficacious in acute, as well as in chronic dysentery. The tincture was prepared according to the formula for tinctures of the British pharmacopœia (2½ ozs. to a pint), and doses of from 2 drachms to ½ oz., were given every four hours.

Bismuthum subnitrate and *salicylin* (Gehe) have been recommended for chronic dysentery in large doses (up to 1·0 every hour) with or without opium. A. Plehn administers the bismuth from the fourth day (calomel previously) 0·5 being given twelve times during the day. Dr. Manson and A. Davidson usually give *oleum terebinthinæ* in gangrenous dysentery when ipecacuanha has proved ineffective. They give 4·0 of the drug daily or on alternate days with 6·0 or 8·0 castor oil, or they administer it every two or four hours in doses of 20—30 drops and a rag soaked with oil of turpentine is simultaneously applied to the patient's abdomen. Fayrer recommends the same remedy in chronic dysentery as follows : 24 drops of ol. terebinthinæ to be given every three or four hours, usually with small doses of opium ; Kartulis recommends it in chronic dysentery when there is tympanitis.

Naphthalin was first used by Rossbach in the treatment of acute and chronic intestinal catarrh (0·1—0·5 several times daily, the maximum for one day being 5·0). Novikoff afterwards ordered it for dysentery. The prescription as ordered by Rossbach was : Naphthal. puriss., sacch. albi. āā 5·0, ol. bergamot., 0·03 M. f. pulv. div. in part. æq. No. xx. s. : 5, 10, 15 or 20 powders daily to be taken in wafers. Kartulis, who gives up to 1·5 per diem, can substantiate the good effects produced by this drug.

Salol was introduced by Rasch for the treatment of dysentery. He gave doses of 1·0 or 2·0, up to 6·0 or 8·0 per diem. It may be given in wafers or dissolved in warm oil, or castor oil worked to an emulsion with gum arabic and water, or, aqua chloroformi, with the addition of a little aq. menth. pip. Fisch and Kartulis observed that favourable results followed the use of salol.

The use of *local medicaments* in the form of enemata, suppositories and the washing out of the large intestine, is often indicated in conjunction with the salol internally.

Enemata of *decoctions of linseed,* or *starch enemata,* with or without *tincture of opium,* are often used for the relief of violent tenesmus. For tenesmus warm sitz baths often render good service.

During the first part of the disease Minerbi used *naphthalin* in the form of enemata several times daily (5·0 with ol. olivæ 20.0).

Fisch strongly recommends *iodoform* enemata in chronic diarrhœa : 0·25 to 0·5 iodoform is well mixed with 1 or 1½ tablespoons of barley or oatmeal water, and the mixture injected high into the intestine by means of a long india rubber tube fitted on to an ordinary enema syringe.

Olive oil enemata (120—240 g.) are recommended by White for constipation.

In obstinate chronic cases Hillier uses enemata of milk.

Astringents and *antiseptics* are especially used for washing out the intestine (enteroclysis). Tannin (0·5—1 per cent.) and nitrate of silver (0·1 per cent.) are especially recommended as astringents, and salicylic acid (1 : 300—1,000) as an antiseptic. Carbolic acid and corrosive sublimate are quite unsuitable for this purpose, being capable of causing symptoms of poisoning.

In order to wash out the intestine, the patient should assume a lateral or knee-and-elbow position, and an india rubber tube (œsophagus tube) well oiled is introduced at least 8 cm. into the bowel, and one or two litres of tepid or warm fluid thrown up. These injections are usually given once or several times daily. They are particularly indicated in *chronic dysentery.*

For acute dysentery, Gastinel recommends that the intestine be washed out with permanganate of potash (0·5—1·0, l.) in addition to treatment by calomel. F. Plehn advises irrigations with a weak infusion of tea, with the addition of red wine, and the subsequent introduction of 1·0 subnitrate of bismuth in 50—100 ccm. water, three to four times daily in the acute stage, and once in the chronic.

Suppositories with *narcotics* such as opium, morphia, extract of belladonna, cocaine, &c., have proved of service in severe tenesmus. Minerbi uses suppositories with *naphthalin* (0·5—1·0 with ol. Theob. 10·0).

In regard to the treatment of *particular symptoms and complications, collapse* is combated by stimulants internally and hypodermics of ether, &c.

Intestinal hæmorrhages should be treated by the application of ice to the abdomen, and the use of enemata with iced water, ergotin and liquor ferri perchloridi.

When *perforation* of the *intestine* is threatening, ice and large doses of opium are ordered. After perforation surgical interference will be necessary in addition to treatment with opium.

Surgical operations have recently been tried in the treatment of dysentery. In Shanghai, according to Zedelius, the tenesmus is frequently successfully relieved by incising the sphincter ani. Stephan and Van Schilfgaarde, in one case of obstinate dysentery, performed colotomy in the left iliac region ; through the artificial anus they successfully treated the diseased parts of the intestine when the artificial anus was closed. Godlee and Balance (*Lancet*, 1895, Dec. 21, p. 1578), also each operated on a case, the patients improved, but subsequently succumbed to other diseases.

For *disorders affecting the liver* local bleeding is recommended ; 10 to 20 leeches are applied to the anus or to the abdomen along the course of the large intestine (Roux).

The *anæmia* and *weakness* remaining after dysentery require the use of iron and quinine and suitable diet ; *paralyses* must be treated by strychnine (subcutaneously) and electricity.

Dietetic treatment is of the greatest importance and should always go hand in hand with other remedies. In *acute dysentery* only *fluid food* must be taken until an improvement occurs. Boiled milk taken lukewarm is the best, and if the patient cannot take it pure, the addition of a little soda water, lime water (a tablespoonful to the cup), or even a little tea, coffee, or cocoa, is permissible.

Where fresh milk is unattainable, unsweetened condensed milk can be given.   Next to milk, gruels and farinaceous foods are recommended, also thin soup, beef tea, meat juice, Leube-Rosenthal's solution of meat, egg water (according to Delioux de Savignac), the whites of several eggs to one litre of water and the addition of a little syr. aurantii.   When the dysenteric symptoms have disappeared, soft boiled or raw eggs, digestible meat foods, &c., may be taken.

As to *drinks*, rice water, barley water, toast water and almond emulsion, all taken lukewarm, will be found most suitable.   Alkaline mineral waters (Vichy, &c.) are well borne by the patients.   Spirits are strictly prohibited.

In *chronic dysentery* a *pure* milk cure is most suitable first of all ; later on its place may be taken by a digestible but strengthening diet.   Fayrer recommends that plenty of bael fruit be eaten ; Fisch advised that a jar of preserved bilberries be taken daily.

In acute dysentery and in exacerbations of chronic dysentery, the patient must be kept in bed and must always be wrapped up warmly. Poultices, hot Priessnitz's compresses on the abdomen, or hot water bottles, render good service.

Warm baths, also, do the patients good, but in using these great care must be exercised to avoid chills.

Finally, it must be mentioned that in chronic dysentery a *change of climate* frequently has good results.   Patients who are unable to return to Europe should at all events try a sea voyage.   Cold and mountainous places are less suitable ; in Egypt the desert (Heluan) is resorted to. After the return home, treatment by waters at one of the spas, Carlsbad, Marienbad, Kissingen, Wiesbaden, or Tarasp is strongly recommended.

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III.

TROPICAL HEPATITIS.

DEFINITION.

Hepatitis is a disease of the liver that occurs principally in warm countries; it is characterised by an inflammatory enlargement of the organ which either resolves or tends to suppuration. The disease either appears *idiopathically* or, which is more frequently the case, *secondarily* to dysentery.

SYNONYMS.

Liver abscess, Hepatic abscess, hépatitis suppurée, suppurante, abcès du foie, hepatitis vera circumscripta s. suppurativa.

HISTORY.

Hepatitis has been known since the earliest period of medical history. The significance of inflammation of the liver was, however, obscure to ancient pathologists, for not only were all diseases of the organs in which pain occurred comprehended under the term, but many other affections of organs in the vicinity of the liver were confounded with it.

We can therefore only regard those cases in which pus formed in connection with the liver as true cases of hepatitis.

Cases of this kind were described by Hippocrates, who even mentions that abscesses were opened by means of the cautery; but it was only in the seventeenth century, during which pathological anatomy began to flourish, that the observations became at all reliable.

Morgagni's investigations have especially served to elucidate the subject of hepatitis. Our knowledge has been still further enhanced during the nineteenth century by numerous reports from medical men who had opportunity to observe hepatitis in warm countries; Twining, Annesley, Budd, Catteloup, Cambay, Haspel, Waring, Morehead, Rouis, Dutroulau, Sachs and Fayrer, have earned distinction in this connection.

GEOGRAPHICAL DISTRIBUTION.

Hepatitis occurs mostly in *tropical and subtropical countries*. India is one of its principal seats, and especially on the Coromandel Coast and on the declivities of the eastern Ghauts is the disease prevalent. In Ceylon it is frequently observed, and it also occurs in Further India, especially in Burma, and in the Malay Peninsula; it is less frequent in Cochin China and in the Chinese ports.

Hepatitis is also common in the islands of the Indian Archipelago, especially Java, Sumatra and Borneo, and in Persia and Arabia, particularly along the shores of the Persian Gulf and the Red Sea.

In Africa the disease is endemic in Algiers, the province of Oran being very severely visited, whilst the province of Constantine on the other hand is but slightly affected. The disease, moreover, occurs in Egypt, Nubia, on the West Coast of Africa, and in Madagascar and Mauritius.

In the Western Hemisphere, the west coast of Mexico, Central America, Venezuela, Peru and Chili are the regions where hepatitis prevails most severely, while it is relatively rare in Guiana and Brazil, and on the Antilles.

Hepatitis is not common in Polynesia, but in New Caledonia a more important centre of the disease has been recorded.

A few tropical regions, such as Singapore, the Sandwich Islands and the Australian Continent, are entirely free, or nearly so.

In the temperate zone, especially in northern and central Europe, hepatitis very rarely comes under observation, though it is not quite so exceptional as was formerly believed. It, however, appears more frequently in South Europe. Ughetti reports the disease from the southern provinces of Italy, Gluck from Roumania, and Marguliës from Southern Russia. It is certain that the "entéro-hepatite suppurée endémique," which, according to Babes and Zigura, frequently occurs endemically in Roumania, belongs to this category.

The geographical region of distribution of hepatitis covers the same ground as that of *dysentery* in all essentials. Kelsch and Kiener justly observe: "L'hépatite suppurée n'a ni foyer endémique ni épidémies propres; partout et toujours elle accompagne la dysenterie." The frequency of hepatitis, however, does not everywhere and always correspond with the prevalence of dysentery; in some countries and in some epidemics dysentery is more often followed by hepatitis than in others. As an instance, dysentery is very common in the West Indies, liver-abscess on the other hand, is almost unknown.

ETIOLOGY.

In accordance with our modern views of inflammation, hepatitis, ending in suppuration, can only be caused by *micro-organisms*, and in confirmation of this opinion the various microbes which are considered to be the excitants of suppuration have been found in the pus of liver abscesses.

Staphylococci, streptococci, diplococci, bacterium coli commune, bacillus pyocyaneus, &c., have all been found in the pus of hepatic abscess, partly in pure cultures, partly combined. In some cases the pus, especially in old abscesses, was found to be sterile, the micro-organisms dying out when the abscesses are of long standing.

The occurrence of *amœbæ* in the pus of hepatic abscesses, and their significance, has been sufficiently explained elsewhere. It frequently happens that the amœbæ are not found in the pus immediately on the abscess being opened, but only after a few days, for they are less likely to be in the pus in the centre of the abscess than clinging to its walls. Kartulis, the principal exponent of the hypothesis that tropical dysentery is due to the amœba, is of opinion that they also play an important part in the etiology of hepatic abscess, the amœbæ invading the liver by way of the portal vein and causing suppuration—not directly—but by introducing suppurative bacteria in their bodies.

But other protozoa have also been discovered in the pus of hepatic abscesses. Thus Grimm, in an indigenous case of liver and lung-abscess, found numerous motile flagellæ, besides many bacteria, and Manson found an *infusorium* resembling balantidium coli, and provided with cilia in the pus of a case in which the abscess had broken through into the right lung.

The micrococci which set up suppuration can reach the liver in two ways :—

(1) From intestinal ulcers they may reach the liver by the portal vein ; (2) or they may reach the liver by the bile ducts. The veins from the bile ducts enter the portal vein, and should the bile passages be ulcerated or blocked, the bacteria that have penetrated from the intestine may reach the liver by this channel (Accorimboni).

It is believed that the hepatic abscesses met with in temperate climates are caused by biliary affections rather than by intestinal lesions. Hepatic infection from *intestinal ulcers*, more especially *dysenteric ulcers*, are, however, of greater importance, forming indeed the most frequent cause of hepatitis. This view was first expounded by Budd, but it was subsequently disputed and has only quite recently again gained more believers. According to Kartulis' observations, which extend over more than 500 cases of hepatic abscess, 55 to 60 per cent. are of dysenteric origin. Zancarol, who reports on 444 cases, observed that dysentery had preceded 59 per cent. Edwards and Waterman compiled 699 cases from literature and in these 524, *i.e.*, 72·1 per cent. proved that dysentery had been the etiological factor. Out of forty-five cases treated in the Seamen's Hospital, Greenwich, between 1870 and 1895, which were compiled by Smith, the autopsy or history of the disease demonstrated dysentery in thirty-eight cases, *i.e.*, in 84·4 per cent. Zancarol and MacLeod call attention to the circumstance, that in patients who during life had exhibited no symptoms of dysentery and who deny having previously suffered therefrom, the autopsy occasionally reveals ulcers or cicatrices indicative of that disease. The percentage of cases caused by dysentery, and which include cases of recovery, are according to statistics, as yet low, so that the confirmation of the theory is dependent solely on cases that have afforded opportunities of *post-mortem* examination.

The more minutely the separate cases are examined, the more limited will the region of the so-called idiopathic hepatic abscess become.

MacLeod attributes the fact of hepatic abscess being so frequently associated with dysenteric intestinal ulcers and so rarely with others, especially typhoid, to the circumstance that the former, in contradistinction to the latter, are often accompanied by *submucous suppurations*.

Hepatitis sometimes follows closely on dysentery, but sometimes weeks, months, or even years (up to ten years, Josserand) elapse before the liver abscess develops.

That dysentery is not the only cause of hepatitis is proved, amongst others, by a case of Buxton's, of multiple liver-abscesses containing amœbæ. The history of the disease did not reveal dysentery, and the autopsy demonstrated no trace of the disease.

Lutz, moreover, does not regard dysentery as a cause of liver abscess, but considers it to be due to a *mucous sanguinolent diarrhœa* that runs a chronic course with frequent relapses and rarely tends to recovery.

The theory requires elucidation on several points which seem to oppose the etiological connection between dysentery and liver abscess.

(1) The great rarity of liver abscess in temperate climates.

(2) The frequent occurrence of the disease in Europeans living in the tropics and its rarity amongst natives.

(3) The fact that women and children are rarely attacked.

(4) The observation sometimes made that hepatitis may precede dysentery.

In regard to the first point, it must be mentioned first of all that dysentery in the tropics is generally more severe than that of temperate latitudes, and above all exhibits a greater tendency to become chronic ; and it is essentially *chronic dysentery* that tends to give rise to hepatitis.

This explanation is, however, not quite sufficient to explain the great

frequency of liver abscess in the tropics and its rarity in temperate climes. *Warm climates* have certainly an important bearing on the prevalence of the disease. As mentioned previously most authors agree that more or less pronounced *hyperæmia of the liver* is apt to develop in Europeans generally soon after their arrival in the tropics from the temperate zone, in consequence of the continuous high temperature. This condition is at first accompanied with increased secretion of bile (sometimes bilious morning diarrhœa), and later diminished secretion of bile, and followed by several subjective disorders. In addition, the Europeans, notwithstanding the fact that their muscular energy and expenditure are apt to be diminished in the tropics, often retain their former style of living. They do not decrease the quantity of food and drink they were wont to partake of, they take too much nitrogenous food, such pungent substances as spices, strong coffee, and above all, spirituous liquors, thereby still further increasing the hyperæmia of the liver. It follows that after every meal temporary hyperæmia and enlargement of the liver occurs, and in the course of years there gradually develops a *hypertrophy of the liver*, that is to say, a hypertrophy of the connective tissue with atrophy of the glandular tissue. The result is that after meals there is a feeling of fulness and weight, sometimes also of pain in the right hypochondrium, symptoms of chronic gastric catarrh, retardation of digestion, constipation, sometimes alternating with diarrhœa, hæmorrhoids, languor, headache, scanty dark urine, enlargements of the liver, &c. An enlargement of the liver due to this cause is designated " *Indian liver*," or " *tropical liver*," by the British, and the condition later on tends to *cirrhosis*. Such hyperæmic or hypertrophic livers are of lessened functional value, and predispose to the development of abscesses.

Of all causes mentioned *alcohol* is the most deleterious, and in the tropics its effects are even more injurious than in temperate climates. Most observers agree that the abuse of alcohol plays an important part in the etiology of hepatitis. According to Manson, 65 per cent. of Waring's liver abscess patients were inebriates. The illness is certainly observed, although rarely in teetotalers, and the fact that the disease is not so frequent at the present time as it was twenty years ago is no doubt owing, at least partly, to the fact that during recent decades the manner of living of Europeans in the tropics has become more moderate. Another reason also is afforded by the improved hygienic conditions having caused a decrease of dysentery. The fact that the French are as a rule, more moderate in their use of spirituous liquors than the English, may account for the disease being less frequent in the French possessions in India (Pondicherry, Karrikall) and in Cochin China. The rare occurrence of liver abscess in natives, as well as in European women and children, is explained in the same manner.

Although the *natives* in the various warm countries suffer as frequently from dysentery as European, and in India even more frequently, it is very rarely that cases of liver abscess occur. The negro race, however, are if anything, more liable than the natives of Asia. According to Buchanan during the years from 1893 to 1896, there were 7,972 cases of dysentery amongst the European soldiers in India, with 441 cases of liver abscess ; there were 79,723 cases of dysentery, and 127 cases of liver abscess between 1892 and 1896 amongst the native soldiers and prisoners. These figures demonstrate that amongst Europeans there was one case of liver abscess to every eighteen cases of dysentery, whereas amongst the natives the proportion was only one case of liver abscess to 628 cases of dysentery.

Generally the cause of this relative immunity of the natives may be ascribed to their abstinence from spirituous drinks. In the larger towns of India and other places where natives have acquired the customs, as also the bad habits of Europeans, hepatitis is more frequent among the native population. Thus Daniels reports that since brandy has become an article of barter with the natives of West Africa, inflammation of the liver often occurs amongst them.

Europeans are most frequently attacked during the first years of their stay in the tropics, though the older residents by no means enjoy immunity. Of 114 cases analysed by Waring, 40 per cent. related to persons who had lived in the tropics for less than four years. In some cases years may elapse after return to a temperate climate before the disease is exhibited.

Reports from all countries coincide in stating that the *female sex* enjoys remarkable immunity from liver abscess, although more frequently attacked by dysentery than the male sex. Of 300 cases reported by Waring, nine, *i.e.*, 3 per cent. only, occurred in women. Of 258 cases compiled by Rouis in Algiers, eight, *i.e.*, 3·1 per cent. were females. Nevertheless, as these numbers are gathered from military colonies, the percentage is decidedly too low. Sach's computation, gathered from a population consisting of an equal number of men and women, is nearer the truth; of 111 Egyptian cases compiled by. this author, six, *i.e.*, 5·3 per cent. only, occurred in females.

As regards *age*, liver abscess rarely attacks children. The cases are more frequent after the fifteenth year, and most of the illnesses occur between the ages of 20 and 40. It is also rarely observed in aged persons.

According to my opinion, the observation made by Annesley that hepatitis sometimes precedes dysentery instead of following it, requires more confirmation, particularly in regard to previous attacks of dysentery from which the patients had recovered. It must also be taken into consideration that, as mentioned above dysentery in some cases has a latent course.

Chills may act as *predisposing causes ;* the maximum number of cases of tropical dysentery, according to Hirsch, occur at the end of the rainy season and during the cold season ; that is, in those periods during which the temperature is subject to the greatest fluctuations, cold nights alternating with hot days. Working in the sun or heat, dietetic errors, excesses in drink or venery, injuries affecting the hepatic region, are all predisposing causes. *Unfavourable hygienic conditions* are also not without influence. According to De Castro, hepatic abscess in Egypt occurs twice more frequently amongst the Greeks, living in unhygienic surroundings, than amongst other Europeans.

According to Smith, hepatic abscesses are also observed in India amongst *horses*.

PATHOLOGICAL ANATOMY.

In the first stage of the disease the liver is enlarged, hyperæmic, dark red or reddish brown and soft. Later on a greyish or yellowish spot about 1 or 2 cm. in diameter, is found on the incised surface of the liver, from which a reddish or slightly purulent fluid exudes. The lobules are obliterated and the hepatic cells become granular, containing drops of fat and grains of pigment. From these *necrotic* patches *abscesses* develop in consequence of further disintegration and suppuration. The contents

of the abscesses rarely consist of pure pus, but are chocolate-coloured, mixed with blood, viscid and thick, and under the microscope exhibit, besides the micro-organism above mentioned, red blood corpuscles, pus corpuscles, *débris* of hepatic cells, shreds of cellular tissue and hæmatoidin and cholesterin crystals. Kruse and Pasquale likewise found numerous Charcot-Leyden crystals. Sometimes the pus is of a greenish colour in consequence of an admixture of bile. The pus has usually no odour, but occasionally the proximity of the large intestine imparts a fæcal smell to it. The wall of the abscess, which is of a symmetrical and almost globular shape, is spongy, and consists of necrotic hepatic tissue, while the process of disintegration is in progress. Occasionally vessels with thickened walls are seen running string-like across the cavity of an abscess. The area around an abscess is frequently hyperæmic and infiltrated, while the remaining parts of the organ mostly exhibit no hyperæmia. When the local process of disintegration has come to a standstill the abscesses are surrounded by a firm fibrous layer that varies in thickness from a few millimetres to several centimetres.

The size and number of abscesses which may be present in any single liver differs.

Two *forms* of abscesses are generally differentiated : (1) The *solitary large abscess ;* and (2) the *multiple small abscesses.* The former is presumed to occur idiopathically, whilst the latter are supposed to develop in conjunction with dysentery. Single abscesses are more frequently observed than the multiple variety. Of 562 cases compiled by Zancarol, 60·2 per cent. were single abscesses and 39·8 were multiple. The difference, however, between the two forms is not absolute, for several large abscesses may often be present, and some one of the multiple abscesses may attain a considerable size. Moreover the solitary abscess may be of dysenteric origin and multiple abscesses may be idiopathic. One particular abscess of the latter category is frequently distinguished by its size and other characteristics as older than the other, so that the more recent abscesses must be regarded as metastases which have come into existence from the older abscess by thromboses of branches of the portal vein. Neighbouring abscesses may intercommunicate.

The abscesses occasionally attain large dimensions. Fayrer drew off by tapping 4·5 kg. of pus out of one abscess. Vaughan operated on a case which yielded 8 litres. It is even possible for an entire lobe or even an entire liver to be transformed into one abscess cavity, the walls of which are relaxed, resembling those of a cyst and leaving but little actual hepatic tissue to be recognised.

The abscesses may be situated in any part of the liver, in the substance as well as on the surface. They are, however, found most frequently in the right lobe, and more especially in its posterior and upper part.

Roux compiled 639 cases, in 453 of which (70·8 per cent.) the right lobe, in 85 (13·3 per cent.) the left lobe, and in two (0·3 per cent.) the lobulus spigelii, was affected. The overwhelming majority of cases in which the right lobe is affected is probably due to the fact of its being much larger than the left one.

Should the abscesses have their seat on the surface of the liver they may form prominences of various sizes.

Frequently the liver is adherent in the neighbourhood of the abscess to the diaphragm, the abdominal wall, the stomach or the intestine.

The *suprahepatic abscess,* as described by Cantlie, is probably either a superficial hepatic abscess which has broken through into the layers of the suspensory ligament or a subphrenic abscess.

The termination of hepatic abscess varies. Apart from being artificially

opened, it may open spontaneously after adhesions have formed in several *directions*:—through the skin, into the abdominal cavity, into the stomach, the duodenum, the colon, the right renal pelvis, the pericardium, the hepatic veins, the right pleura, the right lung, the inferior vena cava. The abscess bursts into the lung most frequently and into the pericardium most rarely.

As to the frequency with which the rupture of the hepatic abscess takes place in various directions the following table, compiled by Rendu, and taken from Roux, gives particulars :—

Authors	Number of Cases	RUPTURE INTO									
		Peri-cardium	Pleural Cavity	Lung	Abdo-minal Cavity	Colon	Stomach and Duo-denum	Bile Ducts	V. Cava	Kid-ney	Ilio-lumbar region
Waring ..	300	—	14	28	15	2	1	1	3	2	2
Dutroulau..	66	—	2	10	7	1	1	--	—	—	4
Rouis ..	162	1	11	17	14	3	6	2	—	—	—
Haspel ..	25	—	4	2	2	—	—	—	—	. —	---
Cambay ..	10	—	—	2	1	—	. —	1	—	—	—
	563	1	31	59	39	6	8	4	3	2	6
	Per cent.	0·13	5·5	10·5	6·9	1	1·4	0·7	0·5	0·3	1

It sometimes happens that the abscess becomes encapsuled and the contents may become caseous or calcified. The general opinion is that in excessively rare cases they *heal spontaneously* through the cavities contracting concentrically, their contents becoming absorbed, the walls coalescing and leaving cicatrices with ray-like processes. Of course it is quite possible, that scars of this kind that have been found at autopsies, and which have been pronounced to be healed abscesses, may really be of syphilitic origin. It must also be borne in mind that in cases of spontaneous cure it is not improbable that recovery has taken place by the pus escaping by way of the bile ducts (Roux).

In regard to the *remaining pathological changes* met with in hepatitis, peritonitis, pleurisy, pneumonia and pericarditis, with their sequelæ, may be found without perforation having taken place, contiguity having caused the inflammation to extend to the various organs in question. The intestine frequently exhibits dysenteric changes. The spleen is found to be sometimes small and sometimes enlarged, owing probably to malarial complications. Sometimes also abscesses are met with in other organs, such as the lungs, spleen, or kidney.

SYMPTOMATOLOGY.

Hepatitis often starts suddenly with an attack of shivering, or a slight rigor. In other cases the disease is preceded by a sensation of indisposition for several days. The rigor is followed by fever, which, however, is not high, and may even sometimes be entirely absent. There is almost always loss of appetite, eructation, nausea, and frequently also vomiting. The stool is usually constipated, but in rare cases there is diarrhœa. The patients, moreover, usually complain of a *sensation of fulness and pain in the right hypochondrium*. The pain is described as

being deep-seated, oppressive, or tense, and is most severe when the disease is superficially situated, whereas, if the abscess be deep-seated it is relatively slight, or may even be entirely absent. A *pain in the right shoulder*, occasionally shooting up to the side of the neck, or through to the shoulder blade, or the upper arm, is almost constantly present. It is of a peculiar dull, nagging character ; according to Fisch, it often feels as if a round spot on the shoulder had been stripped of its skin.

This *shoulder pain* is attributable to the communication between the right phrenic nerve and the branches of the cervical plexus supplying the skin of the shoulder. The phrenic supplies the serous surfaces covering the liver and the parenchyma of the liver itself and the inflammation may thus be communicated from one region to the other (Sachs).

In one case of long standing Rouis observed that atrophy of the deltoid muscle occurred.

Deep respiration causes pain. There is often some dyspnœa and a short, dry, painful *cough* in consequence of diaphragmatic pleurisy, or it may be due to the condition of the liver itself. Finally, nearly all patients suffer from pronounced *insomnia*.

In cases with a favourable course these symptoms may abate in two or three weeks, without the *formation* of an *abscess*. Should the latter develop—which in acute cases occurs during the latter half of the second week, and in subacute cases after from two to four weeks—all symptoms as a rule are augmented. The *fever* becomes more severe and exhibits an irregular, remittent, or intermittent type. It sometimes resembles real intermittent fever, with a quotidian, tertian, or quartan type ; occasionally it is of a typhoid type. The temperature frequently exhibits the character of hectic fever, with attacks of shivering or rigor, alternating with profuse perspirations which frequently assume the form of night sweats. The pains also frequently become more severe. In some cases, on the other hand, the pains decrease, and whereas formerly they were distributed over the entire liver, they now become more localised. The patients in the meantime become emaciated and very weak.

The *objective symptoms* exhibited by the sufferers are as follows : At the first glance they give the impression of being very ill and have a peculiar pale yellowish, clay-coloured *complexion* which, according to Sachs is something like that of a person with jaundice, and partly like the cachectic colouring of a person in an advanced stage of cancer; by Dutroulau the complexion is designated " *pâleur ictérique*." Actual icterus is not frequently observed. The sclerotic is pale and has a peculiar faint glitter which Sachs compares in colour and gloss to that of white wax.

The patients usually assume the *dorsal position*, but slightly inclined to the right, the legs are somewhat flexed and the head bent forward. This position is one in which pressure on the diseased organ is lessened as much as possible.

The *tongue* is covered with a thick yellowish white moist coating.

Respiration is usually accelerated and exhibits mostly the costal type.

The *liver* is without exception *enlarged ;* this is often perceptible on inspection alone and is confirmed by palpation and percussion. The enlargement is either universal or affects only the right lobe. Sometimes even the enlargement is still more limited.

Palpation causes pain and the seat of the abscess can often be ascertained by deep digital pressure. Superficial abscesses can be felt as distinct prominences below the border of the ribs, between the ribs or in the epigastric region. If the abscess is inclined to rupture outwards a

slight œdema is sometimes perceptible over the lower ribs. According to Hassler and Boisson a feeling of deep springiness and elastic tension resembling what is felt on palpating a thick-walled tensely distended india-rubber balloon, is pathognomic of large abscesses.

Percussion proves that the enlargement of the liver takes place first upwards and only subsequently downwards. According to Sachs, this is because the diaphragm offers less resistance to the swollen organ than the other structures in the neighbourhood; this is the case in other acute enlargements of the liver and also of the spleen. The line of dulness as a rule appears slightly convex above, and the mobility of the pneumo-hepatic border varies but little during respiration. The liver also does not alter its position when the patient is turned on the left side, owing to adhesions of the liver to the abdominal wall (Pel.). Sometimes the signs and symptoms consist of a compression of the lung with dulness at the right base and of weakened or bronchial respiration, such as is met with in pleuritic exudations.

Occasionally *pleuritic* and in superficial abscesses also *peritonitic friction* may be heard.

Hassler and Boisson perceived a *friction*, a *fine crepitation* over the hepatic region, especially on inspiration, they were, however, able to prove at the autopsy that it had not proceeded from perihepatitis. According to their view the sound was caused by the œdematous hepatic tissue over the abscess being pressed against the diaphragm during breathing.

The *abdominal muscles*, more especially those of the right side, are frequently found to be rigid on palpation. This, however, is not a pathognomic symptom as it was formerly considered to be, as the same condition is also observed in other painful abdominal ailments.

In rare cases there is distension of the superficial veins of the abdomen, in consequence of the pressure against the abdominal wall exercised by the enlarged liver; there are, moreover, hæmorrhoids, ascites, and œdema of the lower extremities, attributable to compression of the portal vein or the inferior vena cava.

The *urine* is usually diminished in quantity, at first it is concentrated and contains uric acid and urates in excess. When the liver is much diseased, Cayley observes that the secretion of urea is much diminished, and the urine pale, watery, and of a low specific gravity.

Sooner or later the patients die of general exhaustion if no surgical operation is undertaken. In other cases, as we have already seen, there is *spontaneous rupture* of the abscess outwardly or inwardly into neighbouring organs. If the abscess breaks through into the abdominal cavity, the pericardium, the hepatic vein or the vena cava, death rapidly occurs, whereas, if the perforation takes place in other directions the disease sometimes has a favourable issue.

The rupture is sometimes preceded by symptoms that lead one to conjecture what is to follow. Thus perforation into the stomach or duodenum is signalised by obstinate vomiting and convulsive pains in the epigastrium; perforation into the colon by colic and tenesmus, resembling the pains in dysentery; rupture into the lung by the symptoms of pleuro-pneumonia. Swelling and redness at the place on the skin where the rupture will take place outwardly is often observed. Frequently, however, the rupture takes place quite unexpectedly. Then masses of pus more or less stained reddish or reddish brown by being mixed with blood may be coughed up, vomited or passed with the stool or urine. These masses of pus also contain fragments of tissue of all kinds (hepatic

cells, shreds of cellular tissue, hepatised pulmonary substance, and muscular fibres from the diaphragm) and are occasionally voided in the form of little lumps varying in size from a hemp seed to a pea. Should these be discharged into the duodenum, it is usually so intimately mixed with the contents of the intestine, that they entirely escape observation. Sometimes large blood vessels or biliary ducts in the wall of the abscess are opened, so that considerable quantities of blood or bile are discharged outwardly. The fistula which is thus set up may heal, or it may remain permanently.

The rupture of a hepatic abscess into the abdominal cavity causes peritonitis, which in a few hours or days ends fatally.

Should perforation take place into the *pericardium*, violent pains, dyspnœa, and the physical symptoms of rapid pericardial effusion set in ; a fatal issue quickly follows.

The signs and symptoms of liver abscess are not always so characteristic as here described. In more chronic cases, in which the abscesses develop slowly and insidiously, the symptoms may be very obscure. The fever and rigors may be absent, pain over the liver may not be pronounced, and the enlargement of the organ is inconsiderable. The appetite is usually diminished and the digestion disordered, the stools are irregular and sometimes loose. The patients feel unwell, and become thin and weak. Sometimes œdema of the feet sets in. There may be a cough, with some mucous expectoration and slight dyspnœa, so that pulmonary disease is the first thought, especially when, as often happens, friction, fremitus and slight rhonchus at the base of the lung are present. Other cases may be mistaken for malarial cachexia. Frequently it is only *post mortem* that the real nature of the disease is recognised. Encapsuled abscesses may run an entirely latent course and are recognised at the *post-mortem* examination.

The more acute forms are particularly observed in young and strong persons who have not been long in the tropics, whereas the chronic forms occur usually in older residents weakened by the climate.

The *duration* of hepatitis is very variable. In favourable cases without suppuration a cure may be expected in a week or two. In purulent hepatitis also, if the abscess be diagnosed and operated on early, recovery may ensue in two or three weeks. Generally, however, the disease drags on for several months, sometimes for a year or even longer, especially after the abscess has broken through into the lung, when, owing to incomplete drainage, the cavity alternately fills and empties.

The accounts as to the *percentage of mortality* differ considerably, for the statistics sometimes only refer to those cases of hepatitis ending in abscess, and sometimes include those without suppuration.

The plan of treatment adopted also exercises a considerable influence on the mortality ; and the rate of mortality may be different also in different countries. Of 203 cases of liver abscess which Rouis observed in Algiers, 162, *i.e.*, 80 per cent., died. Of 128 Egyptian cases of suppurative hepatitis reported by De Castro, 93, *i.e.*, 72·5 per cent., terminated fatally. According to Morehead, the mortality in the East Indies fluctuated in different hospitals between 14 and 34 per cent. ; in these statistics the non-suppurative cases are included and, as Morehead observes, cases of cirrhosis may also have crept in. Fayrer's reports as to the frequency of hepatitis amongst the English soldiers in the various foreign stations give a still lower percentage. Between 1870 and 1872, 9,615 cases were observed, and of these 461, *i.e.*, 4·8 per cent., terminated fatally. From 1888 to 1891 the number of cases of disease was 4,882, the number of

deaths 329, the mortality therefore being 6·7 per cent. In the Dutch-Indian army the mortality, according to Däubler, fluctuated between 15·3 and 19 per cent. within eight years.

MacLeod wishes to differentiate suppurative and non-suppurative hepatic inflammation from each other, this author being of opinion that they are two different diseases. The former, in his opinion, is always of dysenteric origin.

The *influence of operative treatment* of hepatitis on the mortality is shown by the following statements: De Castro observed a mortality of 76 per cent. in his cases that were not operated on ; in the operated cases the mortality was 48 per cent. Of eighty-one cases, not surgically treated, compiled by the Société médico-chirurgicale of Alexandria, 80 per cent. died ; of forty-two cases surgically treated, 42 per cent. terminated fatally.

Death mostly ensues from exhaustion ; in rare cases it is the result of peritonitis, pneumonia, or other diseases.

As to the *frequency of the various causes of death,* the following statement of Rouis will serve as illustrations. In his 162 cases with a fatal issue, the cause of death was as follows :—

In 125 by the severity of the local process, or from accompanying dysentery.
In 12 by the abscess bursting into the abdominal cavity.
In 11 by the effusion of the pus into the pleural cavity.
In 3 by gangrene of the wall of the abscess.
In 3 by peritonitis due to the hepatic inflammation.
In 3 by the spread of the pneumonia when the pus passed into a bronchus.
In 2 through the rupture of the adhesions with the abdominal wall.
In 2 by intercurrent pneumonia.
In 2 by the pus invading the pericardium.

DIAGNOSIS.

The diagnosis of hepatitis is not difficult in typical cases.

The *gastric symptoms,* the *fever,* the *painful enlargement of the liver,* the conditions made manifest on *percussion, the pain in the shoulder, the sleeplessness,* are symptoms that amply suffice to characterise the disease. As we have seen, however, the signs and symptoms of the disease are not so pronounced in all cases, so that often the diagnosis can only be founded on probability, a definite diagnosis being quite impossible. In tropical practice liver abscess should be thought of in every case of notable deterioration in health, in all obscure cases of abdominal disease that are connected with evening rise of temperature, more particularly when there is enlargement and tenderness of the liver, and dysentery occurs in the history of disease. Pneumonia at the base of the right lung is also always suspicious in a tropical patient.

The *earliest possible discovery of the presence of pus* is of great importance as regards treatment. The commencement of abscess formation is by no means always signalised by rigors. Sometimes it is merely indicated by the fact that the pain which, before, was distributed over the entire liver, is diminished, and a more distinctly marked localised pain obtains. In order to confirm the seat of the abscess, the entire hepatic region must be carefully palpated. Pain, abnormal softness or fluctuation frequently reveal the seat of the disease. Sometimes it is betrayed through vomiting, being constantly induced when pressure is made on a certain spot (Smits).

Exploratory puncture is, however, indispensable for the positive diagnosis of liver abscess ; this is best carried out under an anæsthetic, so that, if necessary, the operation may immediately follow. The operation, if undertaken with due aseptic precautions, presents no dangers ;

even in cases where no pus is found, the consequent bleeding often affords the patient great relief, so that this measure is also recommended for therapeutical purposes.

Exploratory punctures are carried out by means of a Pravaz's syringe with a hollow needle, 10—15 cm. in length, and not too thin, or by means of an exploratory trocar and aspirator. When there is no symptom indicating the seat of the abscess, the puncture is made in the axillary line, in the eighth or ninth intercostal space, about $2\frac{1}{2}$ to 4 cm. distance from the costal margin, and beneath the border of the pleura, the needle being directed up and towards the back; these directions are followed because most abscesses are situated in the upper and posterior parts of the right lobe of the liver.

If no pus is obtained at the first place examined, the puncture should be repeated at other spots. Manson recommends that at least six punctures be made before ceasing the search for pus.

Hassler and Boisson and Powell recommend exploratory laparotomy (at the external border of the right rectus abdominis muscle) as being less dangerous than exploratory punctures.

The following diseases may be instanced amongst others as liable under certain circumstances to be mistaken for liver abscess :—

(1) *Intermittent fever.*—Hepatitis is distinguished from intermittent fever, not only by symptoms directly indicating hepatic disease, but by the lack of malaria parasites in the blood, the absence of splenic enlargement, and the inefficacy of quinine.

(2) *Pleuritic exudation.*—In the differential diagnosis the chief points are to particularly observe the course of the upper margin of dulness. In liver abscess, in contradistinction to pleuritic exudations, a slight convexity which falls off towards the vertebral column is present.

(3) *Subphrenic abscess.*—The history of the disease (previous gastric or abdominal complaints, perityphlitis, &c.), and physical examination for air in the peritoneal cavity is sufficient for differentiation.

(4) *Abscess of the abdominal wall.*—This is recognisable from its superficial position, and more particularly through *Middeldorff's method of investigating tumours* (Sachs). Should a long entomological needle or an exploratory trocar be introduced into an abscess of the abdominal wall, the needle will remain immovable and uninfluenced by respiratory movements. If, however, a liver abscess is punctured the needle will swing like a pendulum with the respiratory movements, its projecting end swinging upwards during inspiration, and downwards during expiration.

(5) *Suppurative hydatid cyst.*—A suppurative echinococcus cyst is capable of causing symptoms similar to those of a liver abscess. The differential diagnosis is principally fixed by the history and by the demonstration of hooklets in the pus removed by exploratory puncture.

(6) *Agglomeration of pus in the gall-bladder.*—This may be easily recognised by the situation and form (pear-shaped) of the painful fluctuating swelling.

(7) *Pylephlebitis.*—The absence of hepatic enlargement (if consecutive formation of abscesses has not taken place) in pylephlebitis, and the signs of septic infection (enlargement of joints, metastases in the lungs, severe disturbance of cerebral activity), of engorgement of the portal vein (ascites, diarrhœa, dilation of the veins of the abdominal walls), and a centre of inflammation in the region of the radicles of the portal vein.

It is easier to avoid confusion with other hepatic diseases, such as

malignant tumours, softened syphilomata, hydatids, dilatation of the gall bladder, all of which are distinguished by a slow and afebrile course.

PROGNOSIS.

The prognosis is a serious one in every case of hepatitis. It is unfavourable when the patients have been weakened by over-exertion, alcoholic excess, previous or contemporaneous diseases, more especially dysentery and malaria.

Should a *simple liver abscess* without complication, be in question, the patient being a strong young person, and should the abscess be recognised and operated on early, the prognosis is, as a general rule, good. On the other hand the prognosis is bad in *multiple abscesses*. The diagnosis of multiple abscesses, however, is always difficult, and if after operation, and with a free flow of pus the fever still persists, the fact that other abscesses exist must be considered probable.

The *opening of an abscess outwardly* affords a good prognosis. When it *breaks inwardly*, the rupture into the lung is the most favourable after that into the large intestine. Perforation into the pericardium or abdominal cavity is fatal.

PROPHYLAXIS.

The principal prophylactic requirements are the thorough treatment of chronic dysentery, leading a regular life, and being especially abstemious in the use of spirituous liquors.

TREATMENT.

At the commencement of the disease the treatment is *antiphlogistic*. Ten to fifteen leeches should be placed on the hepatic region or on the anus (but not if dysentery is present, Roux), and this process is repeated if necessary after a few days. General blood-letting, such as was customary formerly is not now practised. It is only exceptionally, and mainly in the case of strong young people when difficulty in breathing is caused by the pressure of the liver on the lung that moderate phlebotomy is indicated. An *ice-bag*, not too heavy, should be laid over the liver. Inunctions of mercurial ointment, vesicants, &c., are frequently applied. Aperients must, moreover, be administered to the patients, calomel being the most suitable: 1·0 daily in one dose, or divided into three or four doses. Stomatitis should be avoided by thoroughly cleaning the teeth and rinsing the mouth out with chlorate of potash. Attention must be paid to get the bowels well opened, but without inducing diarrhœa; besides calomel, saline aperients will be found to be particularly suitable—Carlsbad salts, Friedrichshall water or Hunyadi-Janos mineral water.

Chloride of ammonium is frequently administered, especially by English medical men : 1·2 morning and evening. Stuart, who was the first to recommend the drug, declares that it even causes absorption of abscesses. Roux and Manson, on the other hand, found it ineffective.

According to Dabney, nitro-hydrochloric acid baths are valuable remedies in all forms of acute and subacute inflammation of the liver, 30·0 of nitro-hydrochloric acid

are added to from 4½ to 9 litres of warm water. Both feet are placed in the liquid, and the lower extremities and hepatic region sponged with it. The bath should last fifteen minutes, and if found too strong the acid must be more diluted.

Narcotics may have to be used to allay *violent pains* and to induce *sleep*.

Should the fever cease and the inflammation decrease without abscess formation, *damp warm compresses* on the hepatic region and *warm baths*, should take the place of the antiphlogistic regimen.

As soon as exploratory puncture has revealed the fact that *pus* has collected in the liver it must be *removed*. For this purpose several methods may be used.

(1) *Puncture drainage.*—At the place where exploratory puncture has yielded pus, a thick trocar such as is used for abdominal puncture is inserted, after an incision 2—4 cm. in length has been made through the skin and the superficial tissues ; in order to avoid the possibility of blood or biliary vessels bursting, or the loosening of adhesions, the pus is allowed to flow out slowly ; a suitable drainage tube or a Nelaton's catheter is then conducted through the trocar, which is then removed. Or the trocar may be left in for two or three days, by which time healing by first intention takes place on both sides of the peritoneum and the puncture-wound is amply canalised. The trocar is then withdrawn and a sufficiently large drainage tube inserted in its place, the wound, if necessary, having been previously enlarged with the knife or dilatation forceps. After puncture the abscess cavity is washed out with a warm weak disinfectant solution (1 per cent. carbolic acid, 0·1 per cent. salicylic acid, ½ per cent. lysol, &c.) ; this, however, should only be repeated when decomposition of the pus sets in. An antiseptic dressing is then applied, which at first is changed twice daily, then once a day, and later more seldom still. Corresponding with the reduction of the abscess cavity the drainage tube is shortened until it can at last be dispensed with, as is done in the treatment of empyæma.

This method, on account of its simplicity, is suitable for private practice, and is especially indicated for weak and anæmic patients, as also for cases in which the suppuration is deep-seated.

Should the flow of pus be insufficient a counter aperture must be made in as deep a place as possible. In case the puncture has been made between two ribs the excision of part of a rib may be necessary for the same reason.

Fayrer has introduced a particular trocar provided with a groove which serves for the introduction of a narrow knife or dilatation forceps for the purpose of dilating the puncture wound.

(2) *The broad stratified incision.*—In abscesses that can be reached from the abdomen below the costal margin the abdominal walls are divided in layers in a direction parallel to the ribs. The liver, when exposed, is fixed to the walls of the wound by a few stitches ; or, if this is impossible, the edges of the abdominal wound are pressed lightly against the liver, or the margins of the wound are packed with iodoform gauze. After the situation of the abscess has once more been definitely confirmed by the hollow needle it is incised, and after the hæmorrhage, which occasionally is considerable, has been arrested by compression, the abscess is washed out with a disinfectant solution, a drainage tube is introduced, the cavity plugged with iodoform gauze and an antiseptic bandage applied.

In abscesses that cannot be reached from below the ribs the opera-

tion must be conducted by way of the thorax, commencing with the subperiostal excision of one or two ribs at the spot where the exploratory puncture has found pus. If not adherent the pleural cavity is then opened. In order to prevent the introduction of air the two surfaces are sewn together or iodoform pledgets are firmly pressed to the upper margin of the wall. The diaphragm is then divided and the abscess incised.

This method is preferable to that of " puncture drainage," but it is more difficult and complicated, and therefore less suitable for private practice.

Should the skin over the abscess be already inflamed, the presence of adhesions may be accepted as a certainty, and the incision can be made at once.

Zancarol, to whom a great quantity of material was available (he observed 562 cases and operated on 316) proceeded as follows : If the abscess was situated in the right lobe of the liver, he opened it with the thermo-cautery, directed by the exploratory trocar ; if it was situated in the left lobe, where there is less danger from hæmorrhage, he used the knife, washed the abscess out with a warm solution of salicylic acid, cleaned the wound with sponges or wadding, plugged the cavity with iodoform gauze, and then applied an antiseptic bandage that was changed on the third or fourth day. Zancarol operated on 157 cases by this method with an average mortality of 29 per cent. In no single case was a fistula left. In forty-one cases, on the other hand, which were incised and drained under antiseptic precautions, he observed a mortality of 62 per cent. and fistulæ in 17 per cent. ; in 120 punctured cases the mortality was 72 per cent. and fistulæ were left in 19 per cent.

Fontan recommends that after opening the abscess, the cavity is to be *scraped out* with a sharp spoon ; by this method he accomplished 86 per cent. cures. Although he says that hæmorrhage need not be feared hereby, the opening of large vessels is quite possible and it would be very difficult to ligature them in the soft tissues of the liver.

Stromeyer-Little *opens* the abscess with one incision. After a trocar has been introduced, a knife is pushed through the trocar into the abscess and the entire thickness of the abdominal wall with the hepatic tissue over the abscess is cut through at one stroke to the length of about 8 cm.

When *fistulæ* remain Rouis recommends the use of sulphur baths ; Aitken advises injections of tincture of iodine.

When the abscess has discharged itself into the lung, inhalations of carbolic acid vapour are recommended.

Should the abscess break into the pleural cavity, the empyæma thus set up should be operated on. When perforation has taken place into the abdominal cavity or into the pericardium, one must endeavour to save life by forthwith opening the part and evacuating the pus.

The sufferer from hepatitis must keep his bed, and his diet must be strengthening but digestible. Hot spices and spirituous liquors are strictly prohibited.

During convalescence the treatment is tonic (quinine, iron, &c.) After recovery, if it is possible, the tropics should be avoided.

When the above-mentioned *chronic enlargement of the liver* exists, regulation of the diet is necessary (moderation, especially in the matter of meat-eating, more poultry and fish than beef and mutton, plenty of fruit, no alcohol). Plenty of bodily exercise should be taken, and there should be systematic use of Carlsbad or Marienbad water. Should this manner of living be of no avail, or should the ailments increase the patient must return to Europe and go through a " cure " at the spas named.

Kohlbrugge (*Arch. f. Schiffs- u. Tropen-Hyg.*, 1898, ii., p. 342) recommends that when there is tropical hypertrophy of the liver, the patient, in order to accelerate the circulation of blood in the liver, should several times daily take *deep inspirations, pressure* being exercised simultaneously on the abdomen.

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IV.

SLEEPING SICKNESS OF THE NEGROES.

DEFINITION.

SLEEPING sickness is the designation of a disease occurring in West African negroes ; it consists of a peculiar somnolent condition, and almost always, sooner or later, terminates in death.

SYNONYMS.

Sleeping sickness of West Africa, Sleeping sickness of the Congo, Congo sickness, Sleeping dropsy, Negro lethargy, African lethargy, Die Schlafkrankheit der Neger, Maladie du sommeil, Maladie des dormeurs, Hypnosie, Hypnose, Malattia del sonno, Somnolenza, Enfermedad del sueno, Doença de somno, Nelavane (of the Wolof), *Dadane* (of the Sererer), *Yela kwa tula, Manungina, Lalangolo, N'tansi* (on the Congo).

GEOGRAPHICAL DISTRIBUTION.

The geographical region of distribution of sleeping sickness is a very limited one, extending over the West African Coast from Senegal to Angola and the hinterland appertaining thereto. The disease, nevertheless, does not occur uniformly, but it exists in certain districts and villages, while neighbouring places are free from it ; thus the disease is very frequent in the cataract region of the lower Congo ; on the other hand, it is unknown at Stanley Pool, which is only a little further inland, and at Banana Point on the neighbouring coast, and on the Upper Congo (Manson). The disease also seems to come and go, and sometimes even appears epidemically. Occasionally entire districts are depopulated, so that in the Congo District negro lethargy is the disease most dreaded next to small-pox.

Besides West Africa, sleeping sickness has been observed on the French Antilles, the Bahamas and in Brazil, but only in negroes who have been brought from West Africa to these places.

Ferguson states that he has also observed the disease in British Guiana, not only amongst the negroes, but amongst the indigenous Indians. Ozzard, on the other hand, did not observe it there, although according to his observations and to Daniels', 60 per cent. of the Indians harbour filaria perstans, with which Manson connects the disease.

We are indebted to Winterbottom for the first information regarding sleeping sickness, he having reported on it at the end of the eighteenth century (1793).

SYMPTOMATOLOGY.

The appearance of the somnolent condition is preceded, often for a long time, by *prodromal signs*, which are so characteristic, that the
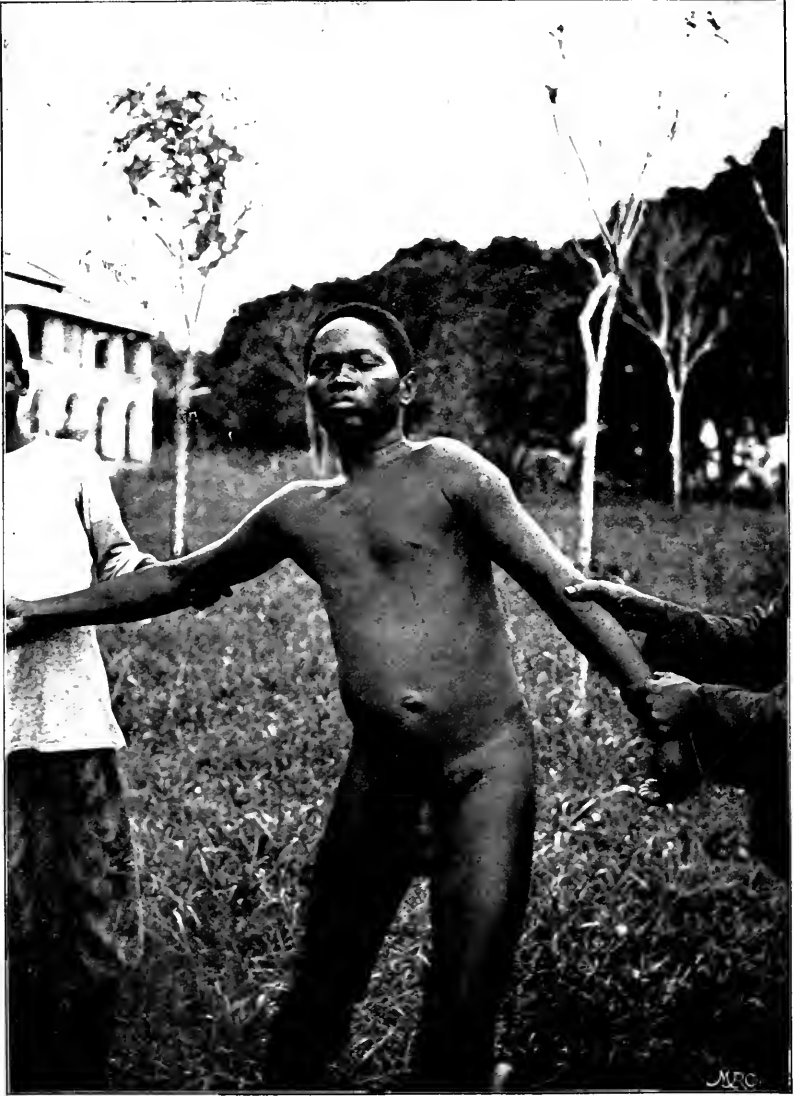
CASE OF SLEEPING SICKNESS.
From the photograph by Dr. HANS ZIEMANN, State Physician, Cameroon, German West Africa.

patient's neighbours cannot possibly be deceived as to the fate that awaits him. The victim complains of weakness, languor, dejection, disinclination for work, headaches, particularly localised over the occiput, a sensation of weight in the head, and giddiness. His eyelids tend continually to close, and he has a tendency to go to rest at unusual hours of the day; for this purpose he seeks out lonely quiet spots, where he spends a long time in dozing. In reference to this, however, it must be remarked that the healthy negro also sleeps a great deal.

Junker v. Langegg says: "The negro works—when forced to—but with frequent interruptions; he eats and drinks, sings, laughs, perspires; he capers and dances with excessive gaiety—or he sleeps. When unemployed, he cannot keep himself awake without a noise. It is therefore customary in the negro schools of the West Indies to oblige the unemployed half of the scholars to sing hymns whilst the other half receive instruction. If this were not done half the scholars would be asleep."

The *inclination to somnolence* can, at the earliest stages of the disease, be resisted to a certain degree, and if loudly addressed the patient will give correct if only monosyllabic replies. If aroused, however, he always relapses into somnolence and the periods of sleep become more frequent and longer, and the waking intervals shorter. The patient's walk becomes unsteady; he staggers about with half-closed eyes like a drunkard. The temperature of the body is lowered, so that the patient feels the want of warmth, and therefore seeks to bask in the sun; the pulse becomes retarded and occasionally, also irregular. Irregular attacks of fever set in periodically, the temperature rising to $38.5°$, $39°$, and even higher, and the pulse becomes more frequent.

During the further course of the disease, the somnolence increases more and more. It is only when the patient is aroused, or when food, for which he never asks himself, is brought to him that he raises himself a little from his resting-place; he sometimes even falls asleep again whilst eating and drinking.

The mental functions of the patients—with the exception of slight loss of memory—usually remain intact. In some cases however, maniacal attacks which exhibit various forms set in; delusions of all kinds, hallucinations, homicidal and suicidal impulses are observed.

The activity of the senses are maintained. The pupils are normal, or are dilated and insensible to light. Strabismus is occasionally present. The conjunctivæ are occasionally injected. The fundus oculi, in all cases submitted to opthalmoscopic examination, was normal (Manson, Corre, Mackenzie).

The muscular power is greatly diminished and there is often severe tremor. Incontinence of urine obtains, and Mense has even seen this condition appear quite early, almost simultaneously with the first symptoms of the disease. In some cases chorea-like movements, general or restricted to one limb, set in, and clonic or tonic convulsions and even epileptiform attacks occur; the latter, however, and also maniacal attacks, are generally observable in cases which run an acute course. The convulsions are usually succeeded by transient muscular spasms or paralyses. The muscular spasms according to Corre, principally affect the sterno-cleido-mastoids and the flexors of the limbs; the paralyses are mostly confined to one side or limb, but paraplegia is also observed.

Sensibility is usually not diminished, or if at all, it is only somewhat decreased during the last period of the disease; sometimes isolated anæsthetic patches are found on the trunk or limbs. The superficial reflexes are as a rule normal. The knee-jerks are present, and rather strengthened than weakened (Mackenzie, Manson).

Cagigal and Lepierre, in one case, found that sensibility was diminished and the reflexes weakened, part of them indeed arrested; the electric excitability of the whole body was diminished.

No disorders can be demonstrated in the internal organs. The urine is normal, the stool alternately loose and constipated; when somnolence is very deep, the stool is passed involuntarily.

Frequently, but not constantly, the *cervical glands* are *enlarged*, and occasionally, also, the occipital and supraclavicular glands. These swellings, which may be present prior to the onset of the disease, are, however, rarely very pronounced; in the multiplicity of cases they never, according to Corre, exceed the size of a bean. They are not generally sensitive. Occasionally, there is enlargement of most of the superficial lymphatic glands.

Sometimes the salivary glands, the parotids and the submaxillary, are swollen and there is increased salivation.

The patients frequently suffer from severe *pruritis*, especially on the trunk; a papular, vesicular, pustular, or impetiginous *exanthem* may appear on the breast and abdomen.

According to Mense, this is caused by the defective care of the skin by the patients, whose cutaneous sensibility decreases more and more.

The alimentary functions, appetite, digestion, nutrition, &c., remain unchanged for a long time. In the last stage of the disease, however, the patient gets thin, and becomes very weak, the pulse becomes small and thin, the skin dry, rough and exfoliatory; slight œdema is occasionally seen at the articulations, or the face becomes puffy; bed sores develop, the somnolence gradually increases to a deep stupor, and death quietly ensues. Sometimes death takes place in an attack of convulsions. Sometimes, according to Forbes, the somnolence disappears towards the end and consciousness returns. Occasionally death ensues from intercurrent diseases, such as dysentery, pneumonia, &c.

Although occasionally evanescent improvements take place, the *fatal issue* is mostly inevitable. Guérin reports that, of 148 cases, all except one terminated fatally. According to Gore, 132 out of 179 negroes who were treated by English doctors on the Sierra Leone coast within eleven years (1846-1850 and 1859-1866) died. Forbes observed thirteen cases, of which eleven had a fatal termination. The result of the other two cases was unknown to him.

The *duration of the disease* is usually between three and twelve months, the average duration being nine months; it may, however, drag on for two or even three years. The care accorded to the patient exercises a decided influence on the time.

PATHOLOGICAL ANATOMY.

Up to the present very little pathological material has been available, as the earlier *post mortems* were not conducted with the necessary care and minuteness, and they only yielded uncertain and uncharacteristic evidence.

According to the most recent examinations by Mott, two of whose cases died and were examined in Charing Cross Hospital, London, it appears that in sleeping sickness it is the question of a *meningo-encephalitis*. Marchoux also found this condition in one case.

The microscopical changes in Mott's two cases were very slight. The *pia mater* was thickened and opaque, the cerebral substance was hyperæmic, and in one case the

cerebro-spinal fluid was increased and slightly opaque, conditions which, in former autopsies, have also been mentioned. The pituitary glands in both cases were normal. Manson, by reason of a case in which he found this gland was enlarged, and had undergone cystic degeneration, with a blood coagulum in or on it, raised the hypothesis that it was there the seat of disease might be sought.

The macroscopical *examination*, on the other hand, conducted by the assistance of modern methods of staining, showed characteristic changes which were most pronounced in the *medulla oblongata*, and at the *base of the brain*. The *pia mater* was infiltrated with mono-nuclear leucocytes, and inflammation continued along the blood vessels and septa into the cerebral substance. The peri-vascular lymph spaces were filled with similar cells, and they were also found distributed in the cortical substance, particularly in the peri-cellular spaces. The ganglion cells (and also those of the spinal ganglia) in one case only exhibited slight biochemical changes (the neuron exhibited no Nissl's bodies, but were evenly stained), which Mott attributes to the hyperpyrexia prior to death, whereas in the other case, in which the patient before death had had many epileptiform attacks, there were numerous ganglion cells with changed and irregular contours. Only a few were normal in the medulla, many were shrivelled and atrophied, whilst others exhibited chromatolysis. In this case there was also atrophy of the nerve fibres in the motor regions of both hemispheres, and a slight diffuse sclerosis of the pyramidal tracts with freshly degenerated fibres. The spinal ganglia in both cases exhibited inflammatory changes.

Mauthner calls attention to the analogy that negro lethargy bears to Wernicke's *acute poli-encephalitis superior*. In this *disease*, the staggering gait, the somnolence, and also the paralysis of the muscles of the eyelids are all present. The closing of the eyes in negro lethargy this author attributes as much to paralysis of the upper eyelid as to the physiological sleepiness of the patient.

Mauthner regards the central grey matter (the grey substance of the cortex of the third or fourth ventricle and of the aqueductus Sylvii) as the seat of disease; according to the hypothesis of this author the disease is originated by the centripetal and centrifugal conductions going through the grey matter being interrupted by the effects of elements of fatigue. In acute poli-encephalitis, a rosy colouration of the central grey matter with numerous small punctiform hæmorrhages, has been found and Mauthner conjectures that in sleeping sickness similar changes being but little noticeable, may perhaps have been overlooked at the autopsies.

ETIOLOGY.

The cause of the disease up to the present time is still obscure. The various hypotheses as to its genesis that have been set up have one and all proved untenable. The following are some of the theories brought forward : a process of intoxication (poisoning by a certain fungus adhering to maize, rice and other cereals, analogous to ergotism ; poisoning by palm wine, Indian hemp ; poison given for criminal purposes). The theory that the disease may originate from emotional distress intimately connected with negro slavery (home sickness, distress of the individual caused by his separation from his family, ill treatment by the slave dealer and planter, &c.), or in consequence of sunstroke. The disease is also attributed to scrofula (on account of the glandular swelling in the neck which exercises pressure on the vessels leading to the brain, and thus are able to cause cerebral anæmia), to malaria or to beri-beri.

The disease has nothing to do with the above-named conditions, nor has it anything to do with so-called " nona," which aroused attention some few years ago and which probably is a question of malaria.

Recently *microbes* have been found in sleeping sickness by several authors, and have been pronounced to be the cause of the disease.

Two Portuguese doctors, Cagigal and Lepierre, in one case discovered a *bacillus* thickened at its extremities and they succeeded in culturing it artificially. By injections of the cultures into rabbits they succeeded in originating symptoms of disease resembling sleeping sickness (sleepiness, emaciation, paresis of the hind-legs, feverishness) which in four out of eleven cases caused death. They therefore regard the bacillus discovered by them as the cause of the disease. Brault and Lapin, who had a

culture of the microbe sent to them and conducted experiments with animals there from, were not able to confirm these observations, and Bullock could discover no microbes either in the blood or lymphatic glands in one of the two above-mentioned cases observed in London.   It appears therefore very questionable if any etiological signification can be attributed to the bacillus found by Cagigal and Lepierre.

Marchoux, in the case mentioned above, found *Fränkel's diplococcus* not in the pia mater but in the pericardium, which was the seat of fresh inflammation ; he likewise found the same micro organism in the secretion of a case of chronic rhinitis which involved the sinus frontalis, the case, however, did not come to an autopsy. Marchoux, therefore regards this diplococcus, which in negroes in Senegal is regarded as being very often, if not always, the cause of several diseases (pneumonia, pleurisy, pericarditis, perimetritis, cerebo-spinal meningitis) as the cause of sleeping sickness ; he, however, offers no explanation why this micro-organism, which is also endemic with us, never creates similar symptoms in Europe.

The hypotheses which connects *animal parasites* with sleeping sickness are founded on equally slender bases.

Manson is inclined to regard the *filaria perstans* discovered by him, whose seat may be in the blood or lymphatic vessels of the brain, as the cause of sleeping sickness.   The geographical distribution of filaria perstans in so far as is at present known, certainly covers that of sleeping sickness.   Manson also found the filaria perstans in five out of nine cases of sleeping sickness (blood slides of which were sent to him from Africa), and also in the two cases observed in London.   When it is considered, however, that this parasite was also found in the blood of 50 per cent. of the healthy negroes, the limitation of sleeping sickness to certain villages and districts whereas filaria perstans is found throughout the entire Congo Valley, the occasional epidemic appearance of the disease, the enlargement of the lymphatic glands that is so frequently observed, and the pruritis that accompanies the disease, all these facts do not coincide with Manson's theory, as he himself confesses.

Embryos during life were found in the blood of the two cases that came under observation in London, and at the *post-mortem* examination parent worms were also found (in the retro-peritoneal tissue and in a pulmonary abscess), but no connection could be confirmed between the parasites and the disease ; and carefully as these cases were examined, they have unfortunately not contributed to the elucidation of the obscurity that clouds the etiology of sleeping sickness.

Forbes, on two occasions found the *filaria sanguinis hominis* in sleeping sickness but he himself regards this as an incidental condition.

Le Dantec regards the embryos of *rhabdonema strongyloïdes* as the cause of sleeping sickness.   This parasite, according to Tessier, penetrates the mucous membrane of the intestinal canal, attains the general circulation and is then retained in the cerebral vessels.

Ferguson attributes the disease to *anchylostomiasis.*   As, however, the occurrence of sleeping sickness in the indigenous Indians of British Guiana has not yet been confirmed, it is questionable if the cases observed by him were really sleeping sickness.

Sleeping sickness is a *disease of the negro race.*   With one or two exceptions—Chassaniol observed it in a mulatto, Clarke in a negro creole boy—it has hitherto only been positively seen in pure negroes, never in other coloured people, nor in Europeans.   As already mentioned, the disease occurs amongst negroes outside their native land, as in the Antilles, &c., but it has never been observed in persons born in Europe, nor in those living there for decades (Guérin).   It is, however, seen two, three, or even seven years after negroes have left their native land.

Sleeping sickness occurs equally in both *sexes.*

No *age* is spared, but persons between 10 and 20 years of age are most frequently attacked.

Occupation exercises no influence.

According to Clarke, the development of the disease is favoured by disorders of circulation, which induce venous engorgement.   Low-spiritedness, insufficient or bad food, suppression of the usual processes of excretion, in fact, all influences tending to weaken the nervous system seem to favour the disease.   According to this author's experience sleeping

sickness is particularly frequent in young girls who have not yet menstruated, or who suffer from menstrual disturbances.

According to Corre, the disease is considered contagious by the negroes generally, and it is particularly the saliva of patients, which they allow to drop into the dish common to the family, that is considered infective. Sometimes entire families are infected. The possibility of hereditary transmission also seems to Corre not to be excluded.

DIAGNOSIS.

The diagnosis of sleeping sickness is easy. Confusion with other diseases is scarcely possible.

PROGNOSIS.

The prognosis has already been sufficiently indicated.

TREATMENT.

Treatment is almost powerless. Attention is chiefly directed to the *feeding of the patients*. If necessary, this must be done *per rectum*. Dried peptones (15·0 : 100·0 several times daily) is particularly suitable for nutritive enemata.

At the commencement of the disease aperients are recommended. Moreover, quinine, arsenic, strychnine (subcutaneously), iodide and bromide of potassium, santonin (Cauvin), stimulants, inhalations of oxygen (Rey), blisters over the cranium, moxa on the neck, cold spongings, inunctions of mercurial ointment, &c., are recommended.

Le Dantec advises *bleeding* (about ¼ litre) weekly, artificial serum to be injected instead, the *rationale* being to gradually free the blood from the parasites, which he considers to be the cause of the disease.

Forbes states that good *results* are attained by *electricity* applied over the spine. This is supposed to stimulate the nervous system.

Various observers recommend treatment with thyroid extract on account of the resemblance of sleeping sickness to myxœdema.

According to Manson, several cases have been cured by injections of *scrotal juice*.

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V.

RUNNING AMOK OF THE MALAYS.

Amok is a *psychical disturbance* occurring amongst the Malays. The person afflicted suddenly runs through the most populous streets of the town or village, brandishing a dagger-like weapon—a cris—carried by every Malay. He even forces his way into houses with open doors, and all that come in his way are struck down, man, woman and child, friend and foe, guilty and innocent, till at last he is secured, living or dead, or he turns the weapon against himself. Sometimes five, ten, or even more persons become the victims of such an attack and are dangerously wounded or killed.

Amok is a Malay word and signifies a frenzied impulse to murder. The person thus affected is called *Orang amok* (*i.e.*, amok man) and the active verb is *Meng amok* (*i.e.*, to make amok, to run amok).

The term amok is often used in an erroneous sense, it being often applied to other conditions, more particularly the outbreaks of fury occurring during inebriation.

Running amok is peculiar to the Malay race, and occurs solely in the Malay Archipelago and on the Malay Peninsula. It is most frequently observed amongst the Buginese, the natives of Celebes. According to Wallace, in Macassar, one or two cases on an average occur every month, and Ellis states that nearly all cases lately observed in Singapore related to Buginese. According to Van Brero, the Madurese, the natives of Madura, yield the most "amok runners" next to the Buginese. According to the official Colonial reports of 1893, cases of amok occured mostly in the provinces of Rembang and Madura.

According to Van Brero, Blandford observed similar cases of murderous attacks in Trinidad in imported coolies. It is ascribed there to the use of *Indian hemp*, and when the culture and importation of the poison was prohibited such crimes became considerably fewer.

Swaving (according to Van Brero) mentions that running amok is especially observed in farmers and mountaineers. It is *never* or *very rarely seen in women*. In former times it was more frequent than it now is, and Van Brero directs attention to the fact that it has never appeared endemically or epidemically.

Unfortunately we have hitherto had no minute account of examinations of "amok runners" made immediately after the attack, so that our knowledge of this highly interesting condition is still very scanty. What we know is as follows :—

The attack is apt to be preceded for several days by a more or less *stupefied condition,* in which the patients give up their usual occupation, avoid communication with their fellow men, sit down and probably brood over something. Ellis states that the Malays, on the whole, have a tendency to a peculiar frame of mind, in which they brood over real or

fancied wrongs done to them, combined with feelings of vengeance. This condition, which in Malay is called *Sakit-hati* (heart sickness) lasts for a few days or weeks ; usually, however, the term is only a few days. Ellis, who saw such patients in the Government Lunatic Asylum in Singapore, compares them to " an ill-tempered child that breaks out into a storm of temper without rhyme or reason." During this condition cerebral functions are retarded and for the time being there is often a lack of memory. According to Ellis, " amok runners " always suffer from such a condition.

Immediately before the attack, according to the unanimous accounts given by the patients, *everything before their eyes is black or red*, everything appears to them to be red as blood ; giddiness also sets in ; they see beasts or devils which they stab down, and then know nothing more. Later on they are apt to say that they have been "*mata glap*" (*i.e.*, my eye has become dark), which is as much as to say " I did not know what I was doing."

During the period of the attack there is *complete amnesia*. The attack as a rule, only lasts a few hours ; sometimes, however, the period of excitement drags on for some few days.

After the attack the patient relapses into a *stupefied condition*, which occasionally deepens into a *deep stuporous sleep* which may last for days ; in this condition the patient is morose, forbidding and taciturn. The short answers wrung from him are, however, correct and connected. According to Ellis they, in addition, exhibit a savage, unearthly, surprised expression of countenance ; the activity of the heart and the respiration are accelerated. The same author states that months after, if much questioned as to their attack, they have a tendency to relapse into the same stuporous condition.

The following *incidental causes* of amok are given. Strong emotion, such as is occasioned by the faithlessness of a wife ; sorrow occasionally caused by the death of a near relation ; grief on account of an actual or imagined injustice suffered ; loss of goods and chattels through gambling ; loss of hope (as on a sinking ship) ; fear of disgrace, as for instance to be taken for a coward ; fear of being imprisoned ; terror; the sight of human blood, particularly his own ; and some feverish conditions, especially malarial fever.

Owing to our imperfect knowledge of running amok it is impossible to express a decided opinion as to its etiology and its place in the classification of insanity ; it is, however, possible to discard a few of the earlier opinions as erroneous.

It has been sought to establish some connection between *Mohammedanism*, to which creed most Malays belong, and running amok on the grounds that the murder of an unbeliever is by the Mohammedans looked upon as a deed pleasing to God. In the Koran, however, no sentence can be found to justify this assertion, and, above all, the amok runner turns his weapon against the faithful and unfaithful alike. In addition, amok running is supposed to have occurred previous to the conversion of the Malays to Mohammedanism (Ellis).

Amok-running has been regarded as a form of *suicide*.

Wallace says : " By the natives of Celebes suicide is regarded as a national and therefore an honourable proceeding, and it is considered the proper way to release oneself from a difficult position. A Roman falls on his sword, a Japanese splits open his abdomen, an Englishman blows his brains out with a pistol, while the Buginese runs amok." This opinion, however, is as a rule decidedly contradicted by the symptoms observed in amok runners before and after the catastrophe.

It may of course occasionally occur that amok is simulated; some one, for certain reasons, may be tired of life and wish to die, and therefore runs amok, whilst quite sane, in the hope of being killed, for according to the ethics of Mohammedanism suicide is a great sin, and is seldom observed amongst the Malays (Ellis).

Heymann held the opinion that running amok was attributable to the *immoderate use of opium.* All modern authors, however, coincide in refuting this idea, and at present the conclusion has been arrived at that the use of opium has by no means the injurious effect on the human body formerly ascribed to it.

In regard to the *use of opium* it is, according to Van Brero, partly smoked (in a particular pipe) and partly eaten or drunk in the Indian Archipelago. Two kinds of opium are distinguished, an expensive kind (called tjandu) and a cheaper kind (tai tjandu, singseng, klellet); the latter is the residue of the former left in the pipe, that is to say, the unburned part of the opium, and it is either smoked over again, or is mostly drunk, mixed with coffee. The smoke of tjandu, according to H. Masson's researches, only contains traces of morphia, whereas in that of singseng, which is whiter and has a sharper smell, pyrrhol, aceton, and the bases of pyridin and hydro-pyridin are found. It is still unknown which element of opium, or its smoke, affords enjoyment; in any case it can hardly be the morphia. Hugh MacCallum even mixed a considerable quantity of morphia with the tjandu of an habitual smoker and found that it diminished the enjoyment. The pleasure does not consist in the traditional "agreeable cloudiness of consciousness with a sensible erotic picture of phantasy" (Emminghaus), but according to N. von Miclucho Maclay, in a condition of profound rest, in which the individual remembers nothing, thinks of nothing and desires nothing, a condition that is so pleasant that he does not wish to be roused from it.

The deleterious effects and the extent of opium smoking, according to competent observers have been much exaggerated, particularly by missionaries. In China, for instance, according to the statistical computation as to the quantity imported, hardly 1 per cent. of the population use opium,[1] reckoning the consumption of each person at 10 to 20 grains daily. It is most harmful to the poorer classes, who use the cheap inferior kinds of opium, more especially from the fact that when they give themselves up to the enjoyment of opium, they do not work, and can earn nothing and are thus insufficiently fed. According to the unanimous observations of the doctors of lunatic asylums in the British and Dutch Indies, opium seldom appears as the cause of mental disorders. Ellis even remarks: I have never yet seen a case of insanity of which I could with any certainty believe opium smoking to be the cause." At the *post mortem* of persons addicted to the use of opium no changes of tissue or organic diseases could be found attributable to that cause (Roberts[2]).

Running amok can also not be said to be due to acute *alcoholic insanity,* for Malays are not addicted to the abuse of liquor, and Indian hemp also, is not much partaken of by them.

Ellis, following the opinion of Bevan Lewis, according to whom every impulsive mental disturbance with pronounced cloudiness of memory is due either to epilepsy or alcoholic delirium, is inclined to regard running amok as a *psychical epilepsy,* although according to his observations ordinary epilepsy occurs relatively rarely in Malays. Van Brero, also, in his practice, did not observe very many epileptics, but on account of the remarkably numerous cicatrices of burns and other wounds which are seen in Malays, deems it possible that there is a greater frequency of this disease than is generally supposed. In order to decide the question of the correctness of Ellis's views, the demonstration of other epileptic symptoms of disease in amok runners would be necessary, and whether one person had had repeated attacks of amok; this has not yet been ascertained.

[1] Müller. Mitt. der deutsch. Ges. für Natur-und Völkerk. Ostasiens., No. 8, 1875, p. 1.

[2] William Roberts. Collected Contributions on Digestion and Diet, with an Appendix on the Opium Habit in India. London: 1897.

Amok-like attacks are observed in *epileptics*. I myself recently had to attend such a case in Europe, which, had the occurrence in question taken place in the Dutch Indies, would certainly have been designated as amok. A man, 30 years of age, quarrelled with some men in an inn, after his peculiar manner had already been remarked in the street. He was turned out of the inn and continued his dispute in the street. After having received several cuffs and blows he drew out his pocket knife, dealt one of his opponents a blow, and then rushed through the street brandishing his knife. He stabbed three perfectly innocent persons that came in his way, and at last was arrested and held fast. Being questioned on the following day, he professed to know nothing of what had happened, he only remembered having been in the inn. When he returned to consciousness he found himself in the police cell. Investigation proved that for sixteen years the man had suffered from frequent attacks of epileptic convulsions as well as of *petit mal*. To this various scars on his tongue gave evidence, as also an attack that took place in prison during the following days.

Rasch considers running amok to be a transitory *mania*, which, according to Kräpelin, is highly probable on the basis of the epileptic theory.

Finally, according to Van Brero, running amok may have *various origins*. It is either a *symptom of insanity* (and according to Van Brero it may occur in any mental disorder, particularly in epilepsy, periodical mania, imbecility and idiocy) or it appears *independently*, or as a transitory psychopathic mental perversion. When it appears independently in persons who have never previously suffered from mental disturbances, but who may undoubtedly be regarded as having perverted minds, this condition may be congenital or acquired. The same causes that contribute to bring about similar transitory disorders may here also come into play, such as intoxication, sunstroke, cerebral and nervous diseases, direct or indirect injuries of the brain, inanition, constitutional ailments (syphilis, febrile conditions, &c.), physiological conditions (as confinements), or emotion. In this respect an important part is played by the want of control of the passions and desires due to the defective training and education of the Malays, who as a race are abnormally excitable.

We see much the same temperament in children when punished. It is a fact also that Malays attach no value to the lives of their fellow creatures, owing, no doubt, to the example set them for ages by their own princes. Malays always carry weapons, so that their use in mental disturbances is but second nature.

The scarcity of running amok amongst women is, according to Van Brero, explained by the fact that in females emotion is indeed quicker, but is not so strong and fully developed as in men, and that above all, in consequence of their subordinate position, they take less heed of annoyances and offences which come in their way, or to which they are submitted.

The question as to the *responsibility* of the person that runs amok is of great importance. One can only agree with Van Brero in asking that responsibility must not be generally affirmed, but that every single case must be regarded separately. For this reason it is requisite that an examination of the patient be made immediately after the attack. Besides the cases in which there is mental oblivion, there may be cases in which responsibility is present or only diminished. Even Ellis allows that sometimes the amok runner, because he wishes to die voluntarily, gives free rein to his passions though he is quite capable of bridling them, and although he is fully aware that it will end in amok.

Ellis, in such a case would make him, at least to a certain degree, responsible for his actions, though he may no longer be conscious of his acts at the crisis of the condition ; just as a man who makes himself drunk

purposely, and then commits a crime in blind drunkenness, must be completely conscious as to what probably will be the consequence of his first intentional act.

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VI.

THE LATAH DISEASE.

Latah is the name given in the Dutch Indies to a form of cerebral neurosis, in which the patients make involuntary movements and incoherently utter sounds or words. The movements are introduced, accompanied or followed by disconnected sounds or words, mostly popular cries, often also obscene expressions (coprolalia). These anomalous symptoms may arise from fright, or may at any time be brought on by other persons making movements before such persons, which are promptly mimicked (echocinesia) and words spoken are repeated (echolalia); orders given are also promptly executed. Occasionally a look, accompanied by a motion of the head, suffices to call forth a few sounds. Ordinary questions which they address to others, distinct paraphasia, or even choreaic paraphasia, is sometimes exhibited.

The movements, exclamations, &c., are quite involuntary. Notwithstanding the most strenuous exertions, the patients are unable to restrain them. In the meantime consciousness is quite clear and the intellect undisturbed. Other disorders of the nervous system are not present, as a rule, and van Brero, whom I principally follow here, could never confirm hysteria or epilepsy in his patients. Sometimes, but not always, there is an increase of the tendon reflexes and an irradiation of the cutaneous reflexes on both near and distant muscles. A symptom common to all patients was that they could be easily alarmed. A few suffered simultaneously from mental disorders, but without any connection between these and latah being apparent.

The disease, which may persist for many years and decades, and which appears to be incurable, occurs principally in *women ;* young women being more frequently affected. *Heredity,* according to van Brero, appears to play an important part.

Latah has indubitably something to do with *suggestion* in persons whose will is weak, so that they are unable to control suggested movements, which are involuntary and which they deeply deplore.

van Brero connects the weakness of will power with the defectvie development of character of the Malays, due no doubt to their neurotic nature and to the oppressed condition in which they are always kept. He defines the disease as *provoked imitative impulsive myosphasm.*

In Java, where the disease is very general, one has the opportunity of observing it daily in the streets. It is principally met with in native women, and occasionally in Indo-Europeans ; it is rarely observed in men and foreign Orientals. van Brero is not aware of its occurrence in other parts of the Dutch Indies. van der Burg mentions that the disease is met with in British India, and there are besides reports

of its occurrence from other countries which geographically and ethnographically are widely separated from one another; for undoubtedly, notwithstanding slight difference in the aspect of disease, latah is identical with *mali-mali* of the Tagalese, the inhabitants of the Philippines; *Bah tschi* in Siam (Rasch[1]); *yaun* in Burmah (Bastian); *myriachit* (Hammond) which exists in Siberia, especially in the neighbourhood of Jakutsh; the *jumping* in North America (Beard). Amongst the Laplanders also, according to Högström, similar symptoms are found.

Gilles de la Tourette's disease, or *maladie des tics convulsivs* (Guinon), which has recently been described from various countries and which mostly comes under observation in *men*, exhibits many similarities with latah, from which, however, it is differentiated by the fact that in it some movements are *spontaneous* and involuntary; but voluntary, symmetrical movements are also present, this is not the case with latah. It may be noted that Beard's jumpers were also principally of the male sex.

Mention must be made also of a neurosis occurring in Japan and which like latah rests on *suggestion*.

In Japan as well as in China,[2] popular belief ascribes to certain animals, such as the dog, the fox, the badger, &c., an important part in these ailments. They believe that the dead—for the Japanese and Chinese have notable powers of presentiment—assume the form of animals in order to appear to the living and punish them for wrongs they have committed; the consequence of such apparitions are diseases—especially mental disorders—for the persons affected. Moreover, the animals mentioned have also the power to transform themselves into other forms, thus they assume the shape of old men, pretty young girls, &c., and thus play tricks on people. Certain persons are suspected to be such transformed animals and all connection with them is avoided.

A disease is attributable to the suggestive influence of this popular superstition, it is frequently observed in the province Tosa on the Island of Shikoku, where it is called *Tanuki gami tsuki* (literally translated, possessed by the badger-god), or *Inu gami tsuki* (possessed by the dog-god).

In persons suffering from this disease the suggestion exists that they are possessed by the badger or the dog; they therefore behave as if they were indeed the *Tanuki gami mochi* (*i.e.*, possessor of the badger-god), or *Inu gami mochi* (possessor of the dog-god), that is to say, persons who are regarded as badgers and dogs in human form, and by whom they have been bewitched; they also assume certain habits of the animals in question, they put their mouths direct to the food when eating, while they place their hands on the ground; they frequently howl and are afraid of foxes, priests, &c.

I extract the following account of a Japanese doctor's observations of such a case from a Japanese medical journal:—

"A girl who had hitherto been quite healthy was playing in a neighbouring house occupied by an old woman who was popularly supposed to be an *Inu gami mochi*, *i.e.*, possessed by the dog-god. She had a rigor, went home and retired to bed. Fever set in, the face was reddened, and had an angry expression and the girl sought continually to hide it under the bed clothes. From time to time she looked around timidly and shamefacedly on all sides with sly glittering eyes. As the girl's father was absent, her grandmother and mother ran and fetched me. When I arrived the girl sat up and looked at me with glistening eyes. Her face was red, the skin covered with perspiration, the pulse accelerated, the eyes shining and immovable, the expression of countenance angry. Her arms were pressed firmly to her bosom and both thumbs bent. According to the popular superstition the animal always invades the human body through the thumbs; the patient therefore always bends the thumbs and to prevent the "spiritual essence" escaping, covers the thumbs with the other fingers, and presses them against the palms. This symptom is present in all cases. She smoked tobacco, drank saki,[3] which she before did not like, and her demeanour was that of an old woman. When I commenced to question the girl she was shy at first, and did not reply. Gradually she commenced to talk and said: 'I do not hate the girl, I only wish to fetch some nasu fruits,[4] out of the house.' I went on questioning her:

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[1] Rasch communicates a short description of Bah-tschi written by a layman (Dr. Frankfurter), according to whom this disease is not identical with latah, as in bah tschi the morbid condition only lasts as long as the patient is bodily touched, "tickled," after which amnesia is supposed to exist for the remainder of the attack.

[2] Compare Otto Stoll, Suggestion und hypnotismus in der Völker-psychologie. Leipzig, p. 34.

[3] Rice brandy, the national drink of the Japanese.

[4] Egg plants (solanum melongea) the fruit of which is eaten.

'What is your name?' She replied smilingly: 'Oh, I am my neighbour, the widow of Muto Shobe, my name is San and I am 76 years old' the name and age were given quite correctly. At this juncture a woman came in to pay a visit and the girl said to her: 'Return the firewood and straw to me; I have waited long enough.' (This woman had actually borrowed these articles from the old *Inu gami mochi*.) The girl's father now returned home. The girl looked at him in surprise and wanted to run away. He, however, bound her firmly to a post, placed a polished lance to her breast and said, 'Return home, or you shall die.' The girl then weepingly replied, 'I will return home and never come back.' Her father then released her and she ran into the neighbour's house and there sank on the floor. She then suddenly awakened and all the symptoms had disappeared. As a rule recovery takes place in this manner. The girl then exhibited passing bodily and mental weakness; for twenty-four hours she suffered from fever and headache; then complete recovery ensued."

The *duration of the disease* is not always so short as in this case, for sometimes it lasts months or years with alternating improvement and deterioration of the condition. Sometimes death ensues from weakness.

The disease occurs chiefly in *women* and *children*, especially in weak-minded, superstitious persons. It is frequently observed during convalescence from such exhausting diseases as typhoid, and also during pregnancy.

Hitherto no more minute observations on this neurosis have been forthcoming.

Suggestion also, perhaps, plays an important part in a peculiar disease called *Koro*, which occurs in the South Celebes and in West Borneo. In this disease the penis now and then exhibits the tendency to retract into the abdominal cavity, and if this is not prevented by the patient or others by firmly grasping the organ, death ensues. The attacks, which are observed in persons with psychopathic tendencies, are supposed occasionally to last for hours, to be accompanied by great terror, and to be followed by great exhaustion. According to van Brero this complaint is attributable to *uncontrollable and frequently returning* illusions, probably founded on superstition.

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V.—CUTANEOUS AND LOCAL DISEASES.

I.

PRICKLY HEAT.

SYNONYMS.

Lichen tropicus, Eczema tropicum, Miliaria papulosa; Der rote Hund; Chien rouge, Eczéma tropical, Miliaire rouge, Roséole sudorale, Dysidrose sudorale, Bourbouilles, Boutons de chaleur, Gale bédouine (Algiers); *roode Hond; Hamonil*, i.e., *Nil eitch* (Egypt); *Ghamachi* (Bengal).

Prickly heat is an ailment with which almost every visitor to the Tropics becomes acquainted on his own person; it is an *acute form of eczema* attributable to increased and permanent secretion of perspiration induced by excessive heat. It is by no means peculiar to the Tropics alone, but also occurs in higher latitudes during the summer. *Eczema æstivum*, which in Europe is observed particularly among children, is nothing more nor less than a slighter degree of this complaint.

The eruption in prickly heat breaks out remarkably quickly. The parts of the skin affected, when superficially observed, look like red patches, but when more minutely examined they are found to consist of innumerable closely set, diminutive, red papules. Upon these small vesicles develop, which usually burst, so that larger or small areas appear quite raw.

According to Pollitzer (*Journ. of Cut. and Genito-Urin. Diseases*, 1893, Feb.) these little vesicles are *retention-cysts* caused by the blocking up of the apertures of the excretory ducts of the sweat glands, owing to the cells of the stratum corneum becoming swollen and obliterating the channels of the ducts.

The complaint may spread over a small or larger portion of the surface of the body. The parts most severely affected are the trunk, particularly the back and shoulders, the forehead, next the arms and backs of the hands, and most rarely the legs and face.

The eruption is accompanied by severe *irritation* of a *pricking* and *burning* character, that increases with every outbreak of perspiration. The itching is frequently so severe that the patient can hardly rest at night. In consequence, prickly heat, though not dangerous, may become a trouble to the healthy, and a serious ailment in the case of sick persons, delicate little children and travellers.

In severe cases *pustules*, *boils* and other forms of *dermatitis* may develop, partly in consequence of the scratching, and partly through septic matter being introduced through the cutaneous erosions, or inoculated by the finger nails.

A particular *pustular* form of the disease is therefore distinguished. It occurs principally in the axillary cavities, round the waist and on the inner surface of

the thighs. The secretion of sweat at these places is greatest, and the possibility of evaporation the least, and the trousers, when worn without braces, chafe the waist. The pustules develop from red papules, which first become vesicular and finally become pustular. They are about the size of lentils or smaller—very rarely larger. At first they cause itching, but later, sometimes on account of the friction of the clothes, burning pains set in. If very close together and they burst, they may become confluent, and form large superficial ulcers as large as the palm of the hand, with uneven edges. The general health in the meantime is not disturbed, there is no fever, and the irritated parts heal quickly under suitable treatment, frequently leaving, however, dark patches on the skin. Nevertheless, Depied, in Tonquin, observed a case with a fatal issue from diarrhœa and fever.

Tribondeau observed the " bourbouilles pustuleuses " in anæmic and feeble persons. Ruge observed eighteen cases on board the ship " Pfeil," off the Zanzibar coast. He attributed their occurrence to the fact that, in consequence of the scarcity of fresh water, those on board the vessel were not able to wash themselves sufficiently with soap and fresh water, but had to be satisfied with sea-water baths ; they were, besides, obliged to wear damp underclothes, impregnated with salt water ; for though the clothes were washed in fresh water they were rinsed in sea water and then hung up to dry. Part of the crew who had had sufficient fresh water to wash in did not suffer from the ailment, which disappeared amongst the others when a sufficiency of fresh water was obtained. Ruge was of the opinion that the continual bathing in sea water and the wearing of clothes washed in sea water, caused the deposit of a certain amount of salt on the skin, the chemical effect of which enhanced the soddening influence of the sweat. Probably the friction of the clothes sufficed to charge the skin with such inflammatory excitants as are always clinging to the cutis.

The *duration* of the disease varies. In mild cases it disappears in a few days. Often, however, in consequence of repeated relapses, it drags on for weeks and months. When cooler weather sets in recovery usually ensues.

The *cause* of prickly heat is found to be the inflammation set up in the skin by the immoderate amount of sweat secreted and left in contact with the skin, and which in addition is loaded with excreted matter (common salt, urea, &c.), the consequence of the diminished excretion of urine.

Europeans are principally affected by the complaint. Personal predisposition, however, varies, and generally depends on the intensity of the sweat-production. Prickly heat by predilection attacks stout and gouty persons, and those who eat largely of nitrogenous foods. In some people the disease returns every year during the hot season. As a rule, however, it becomes milder every year, till after a few years it does not appear at all, the skin appearing to accommodate itself to the effects of heat. Natives are not immune from the disease, but in them the condition is rare. Half-castes are more liable to be attacked than natives. According to F. Plehn, the negro race is possessed of complete immunity.

TREATMENT.

The first necessity of treatment, a treatment also necessary for *prophylaxis*, is *to limit the secretion of sweat as much as possible*. This is accomplished by wearing light, porous, loose clothing. The illness is favoured and augmented by wearing woollen undergarments.[1] Bodily exertion should be avoided, and as little liquid as possible should be imbibed. Only cold drinks, and small quantities of these at a time, should be taken.

[1] For wear in the tropics, smooth, fine cotton singlets are most suitable. Aertex cellular clothing, of which the meshes are not too large, is also highly recommended. For the outer garment cotton materials are also the best.

Cleanliness is the second requirement. The daily bath or sponging so necessary in the tropics, should not be relinquished, even if they cause a transitory increase of the disorder. Undergarments soaked with perspiration should be changed every day. Pearse and Gray condemn the use of soap for baths.

After bathing it is advisable to *powder* the skin with starch, talc, lycopodium or the like, and this should be repeated at bed-time. Manson for this purpose uses a powder consisting of equal parts of boric acid, starch and oxide of zinc.

Fisch advises that after the bath the skin should be *anointed* with borlanolin. Graf's byrolin in tubes is particularly adapted for this purpose. Pearse employs a mixture of lanolin and almond oil (1 : 8).

Sponging with carbolic acid water (1 per cent.), sublimate (1 : 1,000, but only when the disease is limited), creolin ($\frac{1}{2}$ per cent.), sulphate of copper (2 per cent.), chromic acid (2 to $2\frac{1}{2}$ per cent.), borax after the bath, are all recommended.

When pustules have formed they should be opened with a needle or fine bistoury, washed out with carbolic acid water and then powdered. Ulcers should be covered with vaseline.

If the ailment be very severe the patients should be advised to take a change to a cooler climate.

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II.

CRAW-CRAW (KRO-KRO).

CRAW-CRAW (Kro-kro), a word derived from the negro language, is on the West Coast of Africa analogous to the German's layman's expression "Flechte," a collective name for various chronic skin diseases. Most of the diseases thus designated appertain to eczema and scrofula. Unfortunately the term has also been adopted by medical men. I say unfortunately advisedly, because the term is not applied to a certain skin disease, but is used by the same person for various diseases.

Craw-craw is, however, most frequently applied to a *papulo-pustular affection* occurring in negroes ; it has its principal seat on the limbs and trunk, and commences between the fingers, on the wrists and the elbows, whereas the face is but rarely attacked.

First of all, papules the size of a pin's head form ; these are mostly isolated, but are sometimes grouped like a crescent. They appear on the negro's skin, of the same colour as that in their vicinity. After two days, little vesicles develop from the papules, and after two days more pustules form ; these quickly grow large, may become confluent with others close by, and if scratched open and dry up, leave large ugly eschars.

The eruption itches violently, somewhat less in the coolness of the night than in the day, and is regarded as very contagious. Three days are supposed to be the period of incubation.

O'Neil found a little worm,[1] about 0·25 in length and 0·012 in breadth in the papules, but not in the blebs and pustules. Manson, who is the best authority on filariæ, is of opinion that this was a filaria perstans in a somewhat high stage of development. This investigator has therefore brought the disease described above into line with the disease caused by filariæ. Manson's opinion was that the embryos circulating in the blood bore through the capillaries, wander through the tissues and at last settle under the skin, where they originate pustules, and after propagating further escape on to the surface when the eruption is scratched. Recently, however, he has gone back from this opinion. O'Neil's discovery may easily be explained by the fact that owing to the great frequency of the filaria perstans on the West Coast of Africa, it would be easy when cutting off the tips of the papules with a knife for micro-

[1] Nielly (*Bull. de l'acad. de méd.*, 1882, No. 15) found a nematode 0·333 in length and 0·013 in breadth in the efflorescences and blood of a boy, aged 14, living in Miligac, near Brest (Brittany), who was suffering from an eruption consisting of papules and pustules distributed over the trunk and limbs and which itched violently. Nielly regarded the worms as a species of leptodera, but these probably were also filariæ.

scopical examination, as was done by O'Neil, for a little filarial blood to escape from a cut vessel and mingle with the microscopical preparation.

If the patients go to a cooler climate such as Cape Colony, the disease is said to disappear, only to break out again with its former severity on their return to a warm climate.

The disease is very obstinate to treat, sulphur being of doubtful efficacy.

Probably craw-craw is nothing more nor less than *scabies*, and the failure to eradicate the disease is probably owing to new infections.

F. Plehn describes a perfectly dissimilar disease, a *nodular dermatitis* (*dermatitis nodosa*) from the Cameroon Coast, as craw-craw. The disease, which at the lowest computation affects at least two negroes out of every ten, is announced by the appearance of nodules varying in size from the head of a pin to a No. 5 shot, but usually of the size of millet seeds. The nodules are mostly situated on the inner aspect of the thighs, on the scrotum, the inguinal fold, as well as in the gluteal region. The trunk, back, and arms are more rarely affected. The disease is very rare amongst Europeans; it appears on the Tanga as well as on the Cameroon Coast, but is not nearly so frequent in the former locality.

The formation of the nodules takes place in a fairly acute manner, and the further dissemination of the disease occurs, at least during the first period, by means of scratching; the spread is also helped by the coalescence of nodules. In consequence, beet-like flat, hard, infiltrated agglomerations of uneven surfaces are gradually formed, around which small, fresh nodules are gathered.

In the rare cases of the disease in Europeans a slight reddish discolouration is set up during the process; in negroes, in consequence of the copious exfoliation of superficial scales of epidermis, the colour is whitish-grey.

The nodules, examined microscopically, show that they have originated through cellular infiltration and exudation of a highly fibrinogenous liquid into the follicles and sebaceous glands of the skin and neighbouring papillæ.

The disease is infectious. F. Plehn succeeded in inoculating it into healthy negroes by removing matter obtained from the beet-like agglomerations with a sharp spoon and rubbing it into isolated, slightly scarified places on the thighs. He never found filariæ either in the skin or blood, but on the other hand the gland ducts were always choked with staphylococcus pyogenes aureus; nevertheless, he failed to develop the disease by means of inoculations of pure cultures; boils, however, were produced.

The prognosis of this ailment is favourable when energetic treatment is adopted, if not it may persist for months. If the eruption is situated near the eyes it may pass to the conjunctivæ, causing severe keratitis.

F. Plehn found that a 3 per cent. solution of lysol rubbed into the skin for several minutes, after thoroughly bathing and rubbing the affected parts, was most efficacious. Only twelve hours after was the dried-up lather washed off and the procedure repeated. By this method he succeeded in producing a complete cure in a few days in recent patches of the disease, while old sores necessitated a similar treatment for a week or ten days.

ULCERATIVE DERMATITIS—F. Plehn describes another affection—an *ulcerative dermatitis*, which the negroes likewise call craw-craw, but with which he saw only Europeans affected who had dwelt long in the " bush " under unfavourable conditions.

The disease is ushered in by the formation of multiple ulcers varying in size from a sixpence to a two-shilling piece, at a distance of from 1 to 12 cm. from each other and mostly developing on the skin of the leg and thigh, dorsum of the foot and the gluteal region. The ulcers develop from small, red, prominent nodules, on the summit of which sometimes, but not always, a vesicle is seen. The nodules cause unbearable irritation, and are probably ruptured soon after their development by scratching. First small flat ulcerations form, which under the continued influence of the mechanical injury increase in depth and circumference, but they rarely attain a greater depth than $2\frac{1}{2}$ to 3 mm. They are almost always circular in form; more rarely the confluence of two ulcerated edges causes the shape to be irregular.

The spread is undoubtedly due to auto-infection by means of the specific cause of the disease deposited under the finger nails. Whereas, in mild cases, the process may be confined to the legs and the interval between the single ulcers considerable, averaging between 6 to 12 cm., in severe cases the entire lower limbs to the soles of the feet, and also the gluteal region and the nates are affected, and the distance between the ulcers averages only a few centimetres. The ulcers are covered by dark eschars, which are formed by the coagulation of the blood started by scratching. After their removal, discoloured granulations that exude a thin pus are exhibited.

In such cases the condition of the patients is deplorable in the extreme. The disease usually runs its course, attended by intercurrent increases of temperature. Even the epidermis between the ulcers which is not disintegrated becomes eczematous and furuncular through the irritation exercised by the secretion from the ulcers, and from the effects of scratching.

A large uneven infiltration beset with ulcers mostly forms in the vicinity of the nates, so that only a few healthy places can be observed on the diseased parts.

In this condition every position is unbearable to the patient. Defæcation is painful and difficult in consequence of the ulcers on the anus; to sit down causes discomfort; rest at night is well-nigh impossible.

The disease is doubtless of an *infectious* nature. F. Plehn found bacteria of various kinds in the secretion of the ulcers and in the granulations; staphylococcus pyogenes aureus and two fine species of bacilli were always present; experimental transmissions on negroes, however, always proved negative.

The prognosis, even in severe cases, is favourable, but rapid recovery must not be expected. Dark pigmented spots, which sometimes remain for years, are left on the seats of former ulcers.

F. Plehn's treatment consisted in causing the patient to lie on an air cushion, and in particularly severe cases on a wooden stretcher in a water bath; in addition he ordered thorough cleansing of the ulcers and the removal of loose granulations by means of washing them with a pad of cotton wool dipped in a weak solution of acetic acid; the parts were then powdered with oxide of zinc, the inflamed edges anointed with boric vaseline and a tight bandage applied. At the same time a nourishing diet is indicated along with iron or arsenic.

F. Plehn likewise observed a form of *ulcerative dermatitis* on the Tanga coast, especially in negroes. It consisted of multiple cup-like ulcers that mostly appeared on the lower limbs; they were not syphilitic and were cured by scraping and thermo-cauterisation. It does not transpire if the two forms are identical or not.

Emily finally has described an affection as craw-craw that is doubtless identical with endemic *Oriental boil* (see chapter on Oriental sore).

In view of the various applications of the designation craw-craw, it appears desirable that the word should be entirely dropped, and the separate affections thus termed, and which present particular aspects of disease, verified by scientific names, as F. Plehn in some cases has already done.

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III.

TINEA IMBRICATA.

DEFINITION.

Manson designates as tinea imbricata[1], a skin disease that principally occurs in the Malay Archipelago and in the South Sea Islands; it is related to herpes tonsurans, but is caused by a special fungus quite different from trichophyton tonsurans.

SYNONYMS.

Herpes desquamans (Turner), *Herpes farinosus* (Ritter), *Dermatomycosis chronica figurata exfoliativa s. dermatomycosis cærab* (Tamson), *Herpès de Manson* (Roux), *Dajak's schurft, lusung* (Borneo), *Kœrab-besie* (Dajak), *Gune, i.e.,* skin (Gilbert Islands), *Cascado* (Moluccas), *Pita* (Bowditch Island), *Tokelau ringworm, Lafa-Tokelau* (Samoa), *Gogo* (Marshall Islands).

GEOGRAPHICAL DISTRIBUTION.

The geographical region of distribution of tinea imbricata extends over the Malay Archipelago and the South Sea Islands, from Sumatra to the Marquesas and Sandwich Islands.

Which of these islands may be regarded as the actual native land of the disease is not known. We are only aware that during the last few decades the disease has spread from one group of islands to the other in a south-easterly direction. Thus in 1860 the disease was taken from Tamana Island, belonging to the Gilbert Group, to the Tokelau Group, especially Bowditch Island, and it was here called *Pita* after the immigrant named Peter, who brought the disease to the island. From the Tokelau Group the disease was carried to the Samoa Islands, where it received the name of *Tokelau ringworm.*

From the same centre, probably, tinea imbricata also spread to various points of the neighbouring continent, as to the Straits Settlements, —I saw several cases in the Pauper Hospital of Singapore—Burmah and Chittagong. In China (Amoy) also Manson observed the disease, but almost solely in persons who had immigrated from the Straits or Malaya.

In some places the disease is so widespread that the greater part of the population is affected by it.

ETIOLOGY.

Tinea imbricata is due to a particular *fungus* which nestles in the epidermal layers, especially the rete malpighii, whereas the cutis remains

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[1] From *imbrea*, a tile.

untouched. The fungus may be easily recognised, when the scales containing them are treated with a solution of liquor potassæ, as consisting of mycelium threads and spores which both partly contain a dark reddish-brown pigment. It has a great resemblance to *trychophyton tonsurans*, but according to Manson it differs therefrom inasmuch as it is present in much greater quantities, its mycelium threads do not exhibit so many enlargements and contractions, and its spores are usually of an oval shape.

Nieuwenhuis succeeded in *artificially cultivating* the fungus after Kräl's method, and found that a mixture of peptone 2 to 4 per cent., mannite ½ per cent., and agar 2 per cent., or one of peptone, ½ per cent., salt ½ per cent., glucose ½ per cent., glycerine 1 per cent., and Liebig's extract ⅕ per cent., were the best nutritive soils. He also succeeded in conveying the disease to a European by inoculating the culture. The fungus grows very slowly and forms a conglomeration of many, much bent mycelium threads which divide dichotomously and, given a favourable nutritive soil, develop large, light refracting cells or spores at their ends, sometimes two or three in a row.

According to Tribondeau the fungus is not a trichophyton, but should be classified as an *aspergillus*. He found it contained club-shaped sporulating germinal hyphæ but he did not succeed in cultivating it artificially. He gives it the designation of *lepidophyton* (from λεπίς, scale, and φυτόν, a plant).

A warm, moist, even climate, such as obtains in the above-mentioned countries, seems to be necessary for the development of the fungus. During the cool season a remission of the disease usually occurs.

The disease is *infectious*. The transmission takes place either direct from man to man or indirect by means of clothes, mats, &c.

Manson has repeatedly succeeded in experimentally transmitting the disease to the healthy. The first symptoms set in about nine days after the inoculation.

Natives as well as Europeans may be attacked by the ailment. Neither age nor sex has a predisposing influence.

SYMPTOMATOLOGY.

In tinea imbricata the skin is more or less extensively covered by peculiar scales resembling tissue paper ; sometimes, indeed, the entire surface of the body is affected.

Symptoms of inflammation, such as redness, injection, &c., are not usually present, nor have they been exhibited previously. From the very commencement the disease, which takes its point of departure from one or several places, runs its course without inflammatory symptoms. The scales, according to Manson, are about half an inch in length and one eighth of an inch[1] in breadth ; one edge remains free, the other is adherent. In this respect they are different to the scales of other skin diseases, such as psoriasis, pityriasis versicolor, ichthyosis, &c., which are usually attached by the centre. If the diseased portions of the skin be examined more minutely, circular areas will be seen, just as if the disease had started from different centres in parallel and concentric lines. These circles are generally situated ¼ to ½ inch apart. At places where one system of concentric lines touches another, the symmetry is disturbed so that it is barely, or not at all, recognisable. The scales are so arranged that their free ends are towards the centre of the circle or system of circles to which they belong. When the hand is passed over the diseased part, in the direction from the periphery to the centre, the scales are stroked down smooth ; if on the contrary the hand is passed over in the reverse direc-

[1] 1 inch = 2·54 cm.

tion, the scales rise up again and then settle down. It is on this arrangement that the term tinea imbricata is founded.

The greatest amount of desquamation takes place where the diseased parts of the skin are contiguous with the healthy parts. In parts that have long been diseased the scales and circles may be entirely absent and a "piebald" appearance, owing to the pigment being partially lacking, is exhibited.

After recovery the skin remains partly pigmented and partly unpigmented.

As Manson's experimental inoculations show, the disease commences with small, round, slightly raised brown spots which are due to the development of masses of fungi in the layers of the epidermis. While the spot grows towards the periphery, the epidermis in its centre becomes loosened and is shed; in this manner a ring, continually enlarging by peripheral growth, is formed. In this a spot again ensues which is transformed into a ring in a similar manner. Within the second ring a third forms, and so on.

There is no part of the body that may not become the seat of the disease. Certain places, however, are only apt to be attacked after a long continuance of the affection; such parts are the hairy parts of the head, the backs of the hands and soles of the feet, the flexors of the large joints, such as the axillæ, the elbows, the groin and scrotal folds, the popliteal spaces, and the genitals. The hair and nails never participate in the disease, but Manson, in contradiction to other authors, states that as in herpes tonsurans, the hair and nails are frequently affected.

Itching is the chief inconvenience caused by the disease, but the accounts of the various observers differ on this point, some describing the irritation as very severe, some as only slight. Undoubtedly climate and weather influence this symptom as they do the development of the disease. In Amoy, which is not very hot, Manson's patients were only troubled slightly by itching.

The affection is a *very chronic* one, its duration unlimited. Spontaneous recovery never occurs.

DIAGNOSIS.

The diagnosis of tinea imbricata is not difficult. The only disease for which it might be mistaken, or with which it could be confused, is herpes tonsurans. According to Manson the following differences stamp the two diseases :—

(1) Herpes tonsurans, in contradistinction to tinea imbricata, seldom if ever affects the whole surface of the body, or even an entire limb.

(2) Herpes tonsurans, by predilection, attacks the hairy parts of the body, such as the head, the armpits, and the pubes; tinea imbricata, on the contrary, only exceptionally occurs on the hairy parts of the body, and even when attacked the hair is not lost.

(3) Herpes tonsurans is introduced with many more symptoms of inflammation (redness, swelling, formation of blisters, severe itching) than is the case in tinea imbricata.

(4) In tinea imbricata one ring always forms within another, in herpes tonsurans, on the other hand, this is only rarely the case; usually while the ring is enlarging towards the periphery healing is taking place in the centre.

TINEA IMBRICATA.
Straits Settlement. From a photograph by Dr. T. S. Kerr, Colonial Medical Service.

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(5) In herpes tonsurans the scales do not attain the size, nor are they as numerous as in tinea imbricata.

(6) In tinea imbricata usually great masses of fungi are present; in herpes tonsurans, however, the masses of fungi are fewer and smaller.

(7) Inoculation with the scales of tinea imbricata always reproduces tinea imbricata and never herpes tonsurans and *vice versâ*.

(8) Herpes tonsurans occurs in all climates, whereas the geographical region of distribution of tinea imbricata is very limited.

Confusion of tinea imbricata with pityriasis versicolor, psoriasis, ichthyosis and syphilides, is easily avoided.

PROPHYLAXIS.

Daily ablutions of the body, with a plentiful supply of soap, afford the best protection.

TREATMENT.

The treatment consists in the local application of *epiphyticide drugs*, of which *tincture of iodine* and *chrysarobin* (1 : 10—15 vaseline or lanoline, or 1 : 10 traumaticin, the latter especially when the disease is situated in the face) have proved most efficacious. Tincture of iodine is used when the disease is not extensive, and chrysarobin when it is widespread and when the skin is tender (children, Europeans). The application should be preceded by a hot bath with a thorough lather with soft soap and rubbing down with pumice-stone.

Manson found that *iodine liniment*, which he prescribes[1] twice as strong as that of the British Pharmacopœia, had the most decisive results.

Macgregor recommends *sulphur ointment*, and in severe cases *mercurial preparations*.

Bonnafy observed good results from *sublimate baths* (20·0 to 30·0 to the bath), whereas Tribondeau attributes but little effect to this treatment.

Relapses are frequently observed, as isolated masses of fungi easily escape treatment, and then form points of departure of new eruptions. The fungous scales which collect in the underclothes in masses may also cause fresh auto-infection. It is therefore necessary to change and disinfect wearing apparel frequently.

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IV.

PINTA.

DEFINITION.

UNDER the term *mal del pinto* and various other designations, a dermato-mycosis confined to the Western Hemisphere is indicated. It is distinguished by the appearance of spots of different colours which give the patients a piebald appearance, but it causes no disturbance of the general health.

SYNONYMS.

Mal de los Pintos, Mal pintado, Pinto, Mal del Pinto, Peint, Caraté, Cute, Cativi, Tinna, Quirica, Spotted disease of Central America, Pannus carateus (Alibert).

GEOGRAPHICAL DISTRIBUTION.

The disease, according to observations hitherto made, occurs almost exclusively in *tropical countries of the Western Hemisphere*. It has been observed in Mexico, Central America, Columbia, Venezuela, Peru and Chili. It does not, however, appear everywhere in these countries, but is limited to certain regions. In Mexico the complaint rages endemically, more particularly in the province of Valladolid in the vicinity of the volcano Jumello, in Morchoa, and in the provinces of Michoacon, Guerrero—especially in Acapulco—and Tabasco; in Venezuela the disease occurs, particularly in the provinces of Barquisimeto and Merida. It is most largely distributed in Columbia, where it is endemic almost everywhere.

The disease known as *Lota* and which occurs in Surinam (Guiana) and on the Antilles, is perhaps identical with pinta.

Legrain (*Arch. de Parasit.*, 1898, Jan.) has observed a disease in the Sahara that exhibits all the characteristics of pinta.

SYMPTOMATOLOGY.

According to Gomez the appearance of the skin disease is preceded by a *prodromal stage*, consisting in shivering, with subsequent heat, weakness of the limbs, indisposition, headaches, thirst, loss of appetite, severe perspiration, sometimes even emesis and diarrhœa. This condition lasts for four to six days, and about forty days later the spots appear. Gastambide and Iryz do not mention these prodromal phenomena and it seems very questionable if they have any connection with the disease.

As a rule pinta develops very gradually. One or more small *spots*

form on the skin, particularly those parts that are exposed, such as the face, hands, &c. New spots develop near the first ones. The spots enlarge and may become confluent, so that occasionally the entire surface of the limbs is covered by them. No symmetrical arrangement of these spots can be perceived. Their form is manifold as also their colour, which may be *pale grey to black, blue, red* or *white*. At the commencement of the disease the spots on a person exhibit only one uniform colour, but later on, especially when the disease is long standing, spots of various colours are seen side by side. Nevertheless no change of colour of spots takes place; the colour originally seen at the commencement of the disease is retained during its further course. The borders of the spots are sometimes sharply defined and sometimes obliterated. The pigment is sometimes increased in the vicinity of the white spots. The latter, according to Montoya and Flórez, are the consequences of regressive lesions.

The spots cause more or less *itching*, which increases at night with the warmth of the bed, and desquamation of the epidermis takes place; this at first is bran-like, but later the skin is shed in scales of a few millimetres in circumference.

When the disease has lasted some time the skin of the affected parts is dry and coarse to the touch, more rarely moist or greasy; sometimes also it is torn open or even ulcerated in consequence of much scratching.

The patients diffuse a *disgusting odour*, which has been variously described as resembling that of a mangy dog, damp dirty clothes, the urine of cats, or musk.

All parts of the body may be attacked by pinta with the exception of the palms of the hands and soles of the feet. If the hairy parts of the head are affected, the hair becomes thin and white, and at last falls out.

The general health is not disturbed in pinta, but the *disfigurement* caused by the seat of the disease in the face is very distressing to the patient, whose appearance often reminds one of a painted circus clown.

The disease develops very slowly, and its duration is unlimited. It yields to suitable treatment and scrupulous cleanliness, but mild relapses take place. In other cases, however, it may persist for the entire life.

ETIOLOGY.

According to Gastambide's researches pinta is originated by a *fungus*. The microscopical observation of the scales treated with liquor potassæ shows that there is an agglomeration of *spores*, 6 to 8 μ in breadth and 10 to 12 μ in length between the epidermal cells. They are either round or oviform and at the first glance appear to be uniformly black; examined, however, with the light falling obliquely on them these spores will be seen to consist of cells surrounded by a transparent membrane which contains a large number of dark granules suspended in a yellow fluid; the addition of acetic acid makes the presence of the granules plain. In addition to these cells fragments of tubular *threads* are almost always found on which the cells are fixed, something like a cherry on a stem; the filaments, 18 to 20 μ in length and 2 μ in breadth, are white in colour, sharply outlined and appear to refract the light; they exhibit no trace of dichotomy and their base is somewhat broader than the somewhat stumpy tip. When the spots are black and blue, the fungus is situated in the superficial layers of the epidermis; when they are red and white, in the deeper layers; the colours of the spots, according to
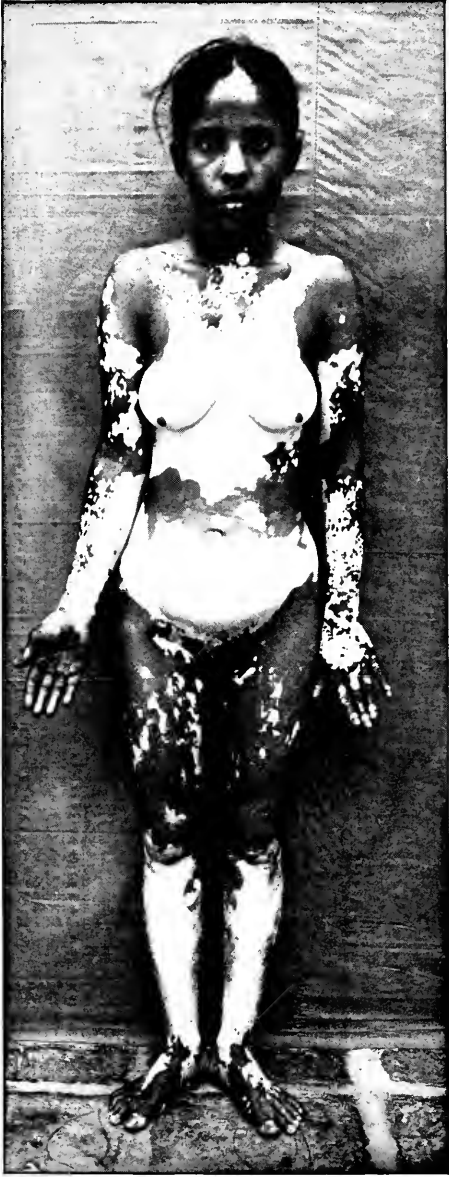
PINTA.
Photographs by P. G. EDGAR, M.B., C.M.
By kind permission of the Proprietors of " The Journal of Tropical Medicine."

Gastambide, are dependent on the different transparency of the unequally thick strata of skin under which the fungus has congregated. According to another opinion the different colours of the spots are caused by different fungi.

A *high temperature and great moisture* is necessary for the development of this fungus, therefore low-lying, warm, damp districts, especially the banks of rivers, are the principal seats of pinta. The disease is aggravated during the hot season and the itching is more severe.

Insanitary conditions, more especially *lack of cleanliness*, are important factors in the development of the ailment. It is to this rather than to racial peculiarities, that the fact is attributable that pinta occurs infinitely more frequently in native Indians, negroes, and half-castes than in whites.

The disease is *contagious* and can also be *carried* from one place to another.

Sex and *age* have no predisposing influence.

DIAGNOSIS.

The skin diseases which under certain circumstances may be confused with pinta are *chloasma, vitiligo* and *leprosy*.

Chloasma and vitiligo spots are distinguised from those of pinta by the fact that they exhibit neither desquamation nor itching. In chloasma, moreover, its connection with pregnancy, uterine disease, and other exhausting diseases must be taken into account. In the differential diagnosis of pinta from leprosy, one fact above all others must be borne in mind, namely, that the spots in leprosy are anæsthetic and are usually accompanied by other symptoms.

TREATMENT.

Before the parasitic nature of pinta had been recognised it was treated by the internal administration of mercurial preparations, iodide of potassium and decoctions of sarsaparilla, although no connection between this skin disease and syphilis was thought of. Gastambide recommends the use of the actual cautery and of blisters. The application of *epiphyticidal* remedies, however, such as chrysarobin, naphthol, sulphur and tincture of iodine, would be more rational.

PIEDRA.—The disease of the hair, known in Columbia (especially in the province of Cauca) under the name of *piedra*, is identical with, or nearly related to, *trichorrhexis nodosa*, which occurs in Europe.

MALABAR ITCH and CHINESE ITCH are nothing more than ordinary *scabies*, in which, in consequence of uncleanliness and neglect, severe symptoms of inflammation have been set up.

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V.

ORIENTAL SORE

DEFINITION.

A CIRCUMSCRIBED inflammation of the skin that occurs endemically in various tropical and subtropical countries, especially of the Eastern Hemisphere, has been described under various names, such as *Oriental sore*, *boil* (sore, evil, bouton, clou, mal) of Biskra, Gafsa, Aleppo, Bagdad, Delhi, Moultan, &c. Notwithstanding the different names only one disease is represented. It is distinguished by a remarkably long course, and is characterised by the appearance of a nodule, the surface of which later on is covered by an eschar, and which is then transformed into an ulcer that finally cicatrises. It seems to me that the appellation *endemic boil disease* is the most suitable for this complaint.

SYNONYMS.

Endemische Beulenkrankheit ; Bouton d'Orient, Bouton des pays chauds, Tubercule d'Orient, (Villemin), *Ulcère d'Orient, Chancre du Sahara, Dermite ulcéreuse circonscrite* (Corre) ; *Salek, i.e.,* annual (Persian) : *Hhab-el-seneh, i.e.,* yearly boil, *Bess-el-temeur, i.e.,* date disease (Arabian) ; *Tschiban, i.e.,* yearly sore, *Dous-el-kourmati, i.e.,* date disease (Turkish) ; *Godownik, i.e.,* yearly boil (Russian) ; *Päschà-chùrdj, i.e.,* fly bite ; *Afghan-jara, i.e.,* Afghan plague, *Jaman dscharagan, i.e.,* malignant ulcer ; *Taschkent-jarassi, i.e.,* ulcer of Taschkent (Taschkent) ; *Mycosis cutis chronica* (Carter), *Lupus endemicus* (Lewis and Cunningham).

GEOGRAPHICAL DISTRIBUTION.

The geographical region of distribution of Oriental sore extends over numerous *tropical and subtropical countries*.

In the Eastern Hemisphere, commencing from the west, it is observed in Morocco, in numerous oases of the Algerian Sahara (Biskra), in the Sahara of Tunis (Gafsa), in the French Congo,[1] in Egypt, Crete, Cyprus, in the Crimea, Asia Minor and Syria (Aleppo), in Mesopotamia (Bagdad), Arabia (Yemen), Persia, the Caucasus, in the Turkmene district (Pendhe), in Turkestan (Taschkent and vicinity, especially along the banks of the rivulet Tschirtschick), in India, in the Punjab (Lahore, Moultan), in the valley of the Indus, in the Rajputana States and in the N.W. Provinces (Delhi).

Juliano has also recently reported its occurrence in Brazil (Bahia).

Within this large region of distribution, however, the disease by no means rages everywhere, but is strictly limited to *certain towns and*

[1] The disease is here called craw-craw (Emily).

districts. This is the reason why the disease is often called after such places.

The first accounts of Oriental sore extend back to the middle of the eighteenth century, and were given by Pococke, Russell, Hasselquist, Holland and Volney, who became acquainted with Aleppo boil in Syria, and reported upon it.

ETIOLOGY.

Oriental boil is *contagious and auto-inoculable to its bearer*, so that it may be spread over the body by scratching. The contagion, as has been confirmed by successful experiments on human beings and animals (dogs, horses, rabbits), is contained in the *nodules* and the *secretions of the ulcers*.

Various authors (Depéret and Boinet, Ducloux and Heydenreich, Riehl, Poncet de Cluny, Brocq and Veillon, Djélaleddin—Moukhtar, &c.) have found *schizomycetes*, particularly certain cocci, in the nodules and the secretions of the ulcers ; it is, however, doubtful if these actually represent the cause of the disease. The most recent researches in this connection have been conducted by Nicolle and Noury-Bey, who cultivated from the blood and pus of the boil a *streptococcus* which was sometimes united in chains, sometimes existed as diplococci. The streptococcus exhibited little virulence in animals, and these authors failed to communicate the disease even to monkeys ; it was uninfluenced by Marmorek's serum. In three cases the streptococcus was found alone, and in six cases combined with other microbes.

The *parasites* and ova of *parasites* which were found by Fleming and Smith, and also Carter's *fungi*, have proved to be mistakes or contaminations.

A former opinion, that the ailment is only contagious in the districts where it rages endemically, but not in other places, has been contradicted by later observations. Depéret and Boinet in France, observed that a battalion of infantry home from Tunis suffering from the disease, carried it to soldiers who had never been in Tunis ; and Kaposi observed that the members of the family of a medical man returned from Euphrates contracted the disease after two and a-half months (Löwenhardt).

The transmission of the disease probably takes place not only direct from man to man, but by intermediate hosts. Flies, mosquitoes and other insects probably play this *rôle*, and the disease may be also spread by washing, by articles of clothing, and by bath water. The connection of the disease with the last named factors is insisted on in Taschkent (Capus). The drinking water theory which was formerly discussed has now been relinquished.

The virus of disease is probably introduced into the human body through *injuries of the integument ;* wounds, abrasions of the skin, scratched insect-bites, eruptions, such as the pustules of acne, impetigo and inoculation, frequently forming the starting point of the disease. As long as the endemic disease is rife, even the most trivial injuries have the tendency to be transformed into these boils.

The *duration of incubation* varies. It generally fluctuates between a few days and a month. In cases in which the disease only breaks out months or years after the affected person had left the infected district, subsequent infection had probably ensued from cocci, which had maintained their virulence in his clothing, &c. When the virus of disease has been directly introduced by inoculation, the period of incubation averages from a few to ten or twelve days.

The fact of having once had the illness does not always afford protection from renewed attacks ; the *immunity* acquired is occasionally only periodical or local, as repeated attacks prove, though it may be said that these are rare.

The disease at various times sets in with unequal frequency, the *seasons* exercising some influence. It is most often observed in the

latter part of the summer and in the autumn; in subtropical regions it occurs from September to November, in the tropics at the commencement of the cool season (Hirsch).

Race, sex, age, constitution and occupation play no part in the etiology of Aleppo boil. All races and classes, every age from childhood to old age, strong persons and weak, all are attacked. The *hygienic conditions*, also, under which the population live have no influence, nor has *food* (dates).

In some places, such as Bagdad, few residents escape the disease; it usually occurs in early childhood, rarely, however, before 2 or 3 years of age. Foreigners are more frequently exempt. Generally ten or twelve months elapse from the period of their arrival before the onset of the disease (Smith); occasionally, however, they are attacked after a stay of from fifteen to thirty days.

The disease is more frequent in *towns* than in the country.

The Oriental boil occurs also in animals, notably *dogs*, in whom the snout is generally the seat of disease.

SYMPTOMATOLOGY.

The ailment starts with a small red spot which resembles the bite of a mosquito. In the centre a nodule of the size of a small hemp-seed forms and gradually increases in size. After this has been present some time a thin fluid exudes from its surface; this dries up and forms a yellowish scab, which being continually contributed to from within becomes larger and thicker. Should this scab fall off, or should it be removed, a small round ulcer is exhibited and this gradually advances at the periphery. Very frequently several nodules surround the first one like a crown, and these are transformed similarly into ulcers which become united to the primary sore. The resulting ulceration, which may attain a diameter of from 8 to 10 cm., is of an oval or irregular shape. Its borders are sharp, vertical, and jagged, as if eaten out; its base is covered by discoloured, hard, indolent granulations, which gradually break down, but are speedily replaced; the vicinity, however, is generally neither inflamed nor indurated. The ulceration exudes a sero-purulent secretion that is sometimes copious and sometimes scanty, at times drying up into a thick yellowish or blackish scab. This sometimes does not fall off but remains sticking till the place is healed; then a round or oval concentric, stratified scab forms resembling a syphilitic sore. After the ulceration has persisted several months without affecting the deeper tissues, healthy granulations appear in its fundus and slow cicatrisation, which as a rule goes on for several months, takes place. Sometimes the centre cicatrises, the process meanwhile advancing at the periphery.

The entire process of disease lasts from a few months to a year and this has given rise to the term " yearly boil," or annual boil, by which the ailment is popularly known in Persia.

The *cicatrix* left is more or less sunken, it is often pigmented and drawn together in a radial manner. This frequently causes disfigurement, especially if situated on the face.

In some cases it does not ulcerate at all. The nodule attains the size of a pea or bean and this disappears again after a few months, followed at times only by a desquamation (Depéret and Boinet's *forme abortive* and *forme desquamante*).

The disease is usually unaccompanied by pain; the patients only complain of more or less troublesome itching at the part affected. Should

the boils be situated on parts with but little subcutaneous tissue, such as the fingers or shins, they may cause severe pain. Disturbances of the general health never occur.

In syphilitic, scrofulous and scorbutic persons the ulcer assumes a malignant phagedænic character (see tropical phagedæna).

The complications observed are as follows : Enlargement of the lymphatic glands, lymphangitis, phlebitis, erysipelas, abscesses, gangrene. Sometimes these may cause death.

The *number* of boils that develop on one patient varies. Sometimes there are only one or two, sometimes ten, twenty, or more, which may be contiguous and confluent, or may be situated on quite different places. Weber observed forty-three boils on one person.

The boils are mostly situated on the *uncovered parts of the body.* The limbs are most often attacked, especially the extensor aspects, next in frequency the face and neck, rarely the trunk and genitals. In the latter case the disease may be mistaken for a phagedænic chancre. In little children the face is usually the seat of disease. It never occurs in the beard, on the hairy parts of the head, palms of the hands, or soles of the feet.

Weber observed 183 cases, in 87 of which the lower limbs were affected, in 73 the arms, in 17 the face and in 6 the trunk.

Emily mentions the frequency of relapses.

PATHOLOGICAL HISTOLOGY.

Pathological researches on Oriental sore have been made by Carter, Riehl, Leloir, Unna, and Kuhn. They all state that it is a *chronic serofibrinous* inflammation.

There is an infiltration of the skin and subcutaneous tissue with small round oval cells, multi-granulated and giant cells, and also a few leucocytes. In the centre of the nodules, over which the epithelium is attenuated, the infiltration is so dense that the tissue elements are entirely disintegrated, while towards the periphery the cells form small centres, mostly situated in the vicinity of blood vessels and lymphatics and sweat glands. The lymphatic vessels and spaces are uncommonly wide and there is much œdema. In the centre of the infiltrated tissue small necrotic particles are enclosed, and this, when the sections are stained, exhibits large fibrinous contents ; the tissue otherwise also contains much fibrin (Unna). Those hairs that still exist are, according to Kuhn, partly broader, partly narrower, occasionally ravelled, and they always exhibit a granular appearance. The root sheaths are sometimes dilated. Here and there the inner root sheaths and to a great extent the outer root sheaths, are also transformed into a shiny mass, probably cornified. In the connective tissue around the hair follicles cavities are found filled with shiny flaky masses which, according to the way they are cut on section, appear of a round or oval form. In consequence of the cornification of the root sheaths no new growth of hair is possible. The blood vessels exhibit endothelial proliferation which may lead to their entire obliteration.

DIAGNOSIS.

The diagnosis of Oriental sore as a rule presents no difficulties. Confusion with syphilis, lupus, scrofula and leprosy are easily avoided, especially if the lack of other ailments as well as the history of disease are taken into account. Geber, nevertheless, states, on the grounds of his experiences gathered on a journey through the East, that in the Orient there is much abuse of the diagnosis " Aleppo boil," and syphilitic, lupous and scrofulous affections are confused with it.

PROGNOSIS.

The prognosis, as a rule, is *favourable,* if one excepts the disfigurements that are apt to ensue from contraction of the cicatrices, especially on the

face. Death rarely results, but should it occur it is due to some inter-current complication, especially erysipelas.

PROPHYLAXIS.

If the opinion be correct that the virus of disease penetrates into the human body through the skin, the greatest protection from the disease will be afforded by the most scrupulous cleanliness, frequent ablutions with soap, care in avoiding injuries of the epidermis and, in case of such injuries occurring, their careful treatment.

TREATMENT.

During the first stage of the disease some authors recommend *cauterisation* with nitric acid, carbolic acid, caustic potash, sulphate of copper pencil, but above all with the actual cautery, whereas other authors denounce such treatment as injurious. *Scraping out* the nodules with the sharp spoon and also *excision*, have been resorted to. Most observers, however, advise an *expectant* treatment.

Should the ulcer be covered with a scab it should not be removed, but protected by a simple bandage, for experience teaches us that the ulcerations heal well under such scabs. Ulcers should be bandaged antiseptically, or treated with such ointments as boric, salicylic or iodoform. Powders also, such as calcined alum, should be used in order to induce the formation of eschars. Emily achieved favourable results with boracic acid, which, after previous thorough disinfection with sublimate, is dusted thickly over the ulcers, which are then covered with a tight bandage.

In order to shorten the duration of the disease, the removal of patients from the region of infection is indicated.

A peculiar " boil " disease that occurs in Bucharest and which is designated *Bucharest boil*, is not identical with the ailment described above. Finkelstein[1] describes its clinical course as follows:—

A painful nodular induration appears on any part of the body subsequent to sensations of pain ; after two or three weeks the lump exhibits fluctuation, and intermittent fever with rise of temperature up to 40° develops. After the abscess has been opened it heals in from one to three weeks, leaving a contracted cicatrix, sometimes also articular anchylosis. These abscesses may attain the size of a child's head, containing as much as 2½ kg. of pus. They are mostly situated in the region of Scarpa's triangle, or in the lumbar region. The general health is but little disturbed ; the lymphatic glands in the diseased region are also but slightly enlarged. The disease rarely leads to a fatal issue.

Strong persons between the ages of 18 and 35 are mostly attacked. Whereas the native population of Bucharest suffer severely from the disease the immigrant Russians escape, probably owing to the better sanitary conditions under which they live. There is no direct contagion. The bacteriological examination of the pus and blood exhibited larger numbers of Fränkel's pneumococci in the pus and occasionally streptococci and staphylococci. The blood contained no malaria parasites.

According to Finkelstein the deplorable sanitary condition of the town of Bucharest considerably conduces to the spread of the boil ailment. It has no connection with plague.

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VI.

ULCERATING GRANULOMA OF THE PUDENDA.

DURING the last few years a new venereal disease has been described under various appellations, such as *groin ulceration, sclerotising granuloma of the pudenda, chronic venereal sores, das venerische granulom ;* it is distinguished by its granular character, its great extent, and its exceedingly chronic course.

The first publication (1896) came from Conyers and Daniels, who observed the disease in British Guiana in *negroes* and *East Indians ;* Daniels also observed it in the Fiji Islands, in the Melanesians of the New Hebrides and the Salomon Islands. Soon after reports followed from the East Indies themselves from Maitland, MacLeod, &c. Manson also made a communication on the subject. Goldsmith had also seen the disease in Northern Australia (Palmerston) in two indigenous women (Bibras), in a *negro* who had had sexual intercourse with them, and also in a *white man* who was in the habit of having connection with a native woman. Probably also the disease observed by Dempwolff in New Guinea in Melanesians and Papuans, was of this nature.

The disease presents itself as a light-red, shiny mass of granulation tissue that easily bleeds ; it is of various sizes, exudes a thin light sanguineous fluid and exhales a fœtid smell. The granulations are largest at the margins, the centre appearing rather sunken. The granulations also appear to be strongly developed in the hairy parts of the body. The secretion differs ; sometimes it is so great that it runs down in drops, in other cases, on the contrary, it is scanty, and then the masses of granulation are covered with drying scabs. Sometimes the granuloma heal in places by shrivelling up, leaving firm raised hairless cicatricial tissue with a thin epidermal integument, and which is in parts lighter, in parts darker than the skin in the vicinity. Sometimes these cicatrices lie like islands in the masses of granulation ; sometimes cicatrisation occurs at one side and the disintegrating process advances on the other. In consequence, also, of cicatricial contracture, the contiguous skin may be drawn away Complete spontaneous cure is, however, rarely or never observed, and the cicatricial tissue that has formed soon again becomes disintegrated.

As a rule the *genitals and contiguous parts,* the pubes, abdomen, inguinal region, thigh, perineum, vicinity of the anus, as far as the coccyx and buttocks, are the seat of the disease.

In exceptional cases the disease is observed on other parts of the body. Maitland in one case saw it on the inner surface of the cheek, in another case on the inner surface of the lips, gums, and side of the tongue, and the wife of one patient presented a similar affection of the mouth.

The disease, according to Conyers and Daniels, commences with a nodule, in men mostly on the pubes or in the inguinal region, sometimes also on the prepuce or the glans penis ; in women it commences on the labia or in the vagina, while, according to Maitland, a chancre or a suppurating bubo following a chancre always forms the starting point of the disease.

The spread of the disease takes place partly by continuity, partly by contiguity.

From the skin the disease may reach the mucous membranes, as from the penis to the urethra, from the labia pudenda to the vagina, from the vicinity of the anus to the rectum, and *vice versâ*, and strictures of the rectum and urethra may be set up in consequence of cicatrisation. As a rule, however, the process is confined to the superficial tissues, to the skin and subcutaneous cellular tissues, and does not penetrate deeper. Fowler alone mentions a case in which the disease passed from the left groin to the bladder, which resulted in the formation of a urinary fistula. An elephantiasis-like condition sometimes develops on the penis and scrotum without any complication with filarial disease being present.

The spread of the disease is slow, even in cases when it was rapid at the commencement, so that the process extends over many months or years. In a few patients it had persisted ten years and even longer.

The corresponding lymph glands do not participate in the disease.

The ailment causes no suffering. Even the general health is either but little disordered or remains unaffected. It is only in severe cases of long duration that the patients become anæmic and enfeebled in consequence of the considerable discharge, and finally succumb to exhaustion.

Galloway, who received the material from Daniels, reports that according to histological researches the granuloma appertains to the *infectious granulation tumours*. The disease commences with a small-celled infiltration in the upper part of the corium and in the papillæ ; the interpapillary epidermal processes then increase considerably in length and the connective tissue of the corium disappears, so that large masses of the small-celled infiltration lie under the elongated epidermic cones. The cells are mostly plasma cells, not ordinary leucocytes. The epithelium of the surface is very thin and atrophied and is absent in places. The vessels of the cutis are widely dilated. The glands in the deeper strata of the cutis and subcutis are mostly normal ; some, however, exhibit cystic dilatation. In the older parts of the neoplasms newly-formed connective tissue is found in place of the cells. The infiltrated masses exhibit no tendency to caseation nor do they contain giant cells.

The disease is *contagious* and, as the above-mentioned spread by contiguity proves, it is *auto-inoculable on the bearer*. However, experimental transmissions conducted by Conyers and Daniels on guinea pigs had negative results. The unknown virus of disease is undoubtedly contained in the secretion from the granulations. The seat of the ailment on the genitals and the frequent primary affection of the penis in the male and the vagina in the female, combine to indicate a disease of a *venereal character*. Nevertheless, it has no connection with syphilis, this being proved by the inefficacy of anti-syphilitic drugs. Complications with syphilis, however, occur occasionally. Maitland's observations point to the probability that venereal ulcers may form the point of entrance for the disease.

The disease is mostly observed in *adults*, never before puberty.

As has been gathered from the few reports published, the disease occurs in the most diverse races. Race therefore plays no essential part in its etiology.

The *diagnosis* of pudendal granuloma should usually present no difficulties. It is particularly distinguishable from soft chancre and syphilitic affections by its granular appearance, its great extent and, above all, by its chronic course. It is also not difficult to differentiate it from Oriental sore and yaws.

The *treatment* consists in scraping out the masses of granulation with subsequent cauterisation, for which purpose the thermo-cautery, chloride of zinc, sulphuric acid, Vienna paste, &c., may be used. Bandages with antiseptic solutions are then applied. The excision of the entire granular and cicatrised mass is also recommended. Conyers and Daniels achieved good results from acidi salicyl. 1·8—2·4 to 30·0 ungt. creasoti.[1] Daniels also found that large doses of iodide of potassium (1·8—2·4 three times a day) was not entirely without effect, as it assisted any tendency to cicatrisation.

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[1] The ungt. creasoti of the British Pharmacopœia contains 1 creasote to 8 adeps.

VII.

TROPICAL SLOUGHING PHAGEDÆNA.

DEFINITION.

The malignant ulcers of the skin, which under certain etiological conditions are frequently observed in the tropics, are comprised under the term *tropical phagedæna*. Formerly the disease was described under various local designations, such as *ulcer of Yemen, of Aden, of Cochin China, of Annam, of Mozambique*, but each represents the same process of disease. Opinions are divided as to whether the atonic phagedænic ulcers occurring beyond the tropics with equal frequency, though not with equal malignancy, are related or identical with tropical phagedæna, or if it be a disease *sui generis*. According to the reports of cases in the East Indies I agree with Corre and Roux in believing the ailments to be identical.

SYNONYMS.

Der Tropische Phagedänismus ; Ulcère phagédénique des pays chauds ; Ulcère phagédénique endémique, Phagédénisme des pays chauds ; Sarmes or Sarnes (Congo).

GEOGRAPHICAL DISTRIBUTION.

Phagedæna has been observed in almost *all tropical countries* of the Old and New World. There are reports as to its occurrence on the West and East Coasts of Africa, in the Soudan, in Madagascar and the neighbouring islands, on the coasts and islands of the Red Sea, in India, Cochin China, Annam, China, in the Indian and Pacific Archipelagoes, in Mexico, in Central America, Guiana and the Antilles, sub-tropical countries, such as Algiers, Egypt and South Africa, are also visited by the disease. I had the opportunity of seeing a great number of cases of this disease in the hospitals of Singapore and Batavia.

In isolated strips of land, such as in Cochin China and on the coasts and islands of the Red Sea, the disease appears to rage with peculiar malignancy, on which account it has been designated by the name of such places (see above).

ETIOLOGY.

It can hardly be doubted that *micro-organisms*, specific or various, are the cause of phagedæna. It seems, however, very questionable if in the bacilli found by various investigators (Le Dantec, Petit, Boinet, Blaise, Crendiropoulo), not reckoning the ordinary suppurative and putre-

factive fungi, the actual cause of the disease has been discovered, or these organisms are only present as secondary invaders.

Le Dantec's *bacilli* were on an average 7 to 12 μ in length, and were sometimes bent ; they were immobile, did not stain by Gram's method and could not be cultivated on the ordinary nutritive media. Blaise also found long *bacilli*, some of them bent, pure cultures of which he could not obtain ; whereas Crendiropoulo regularly found a *bacillus* with rounded ends, which was two or three times as long as it was broad ; it exhibited spontaneous movement, and was easily stained with basic aniline stains, but was decolourised by Gram's method. It could be artificially cultured and within twenty-four hours it liquefied the gelatine around the inoculatory puncture ; in twelve days all the gelatine was liquefied. Bouillon cultures became strongly alkaline and exhaled a putrid odour. Inoculation of rabbits and pigeons with this bacillus killed the animals or gave them blood poisoning. After weaker inoculations a phagedænic sore was set up at the place of inoculation which began to cicatrise after three weeks.

Opinions as to the infectious nature of the disease differ. In contradiction to the earlier opinion that phagedæna is not contagious, Le Dantec and Blaise have recently pronounced it infectious, although the latter inoculated himself with the pus with a negative result, and could only produce uncharacteristic ulcers in guinea pigs ; earlier inoculatory experiments were also futile. Le Dantec identifies tropical phagedæna with the *hospital gangrene* of temperate climates, which, thanks to the antiseptic treatment of wounds, has now become remarkably uncommon, while Blaise as well as Brault assert that the former disease may be complicated with the latter. It follows therefore that further research is required for the elucidation of this question.

The prevalence of phagedæna in the tropics is certainly suggestive of a pathogenic influence by the *climate*, particularly in regard to the high temperature and the great moisture of the air. This influence is still further proved by the fact that the disease is principally observed during the hot and rainy season, and is also met with more frequently in low-lying damp strips of land, on the sea shore and the banks of large rivers and in marshy districts rather than in the higher and drier regions of the interior (Hirsch).

An important part is played in the etiology of tropical phagedæna by a weak state of health, such as may be induced by unfavourable hygienic conditions (insufficiency of food, defective dwellings, uncleanliness), chills, great bodily exertion, preceding or existing diseases, such as malaria, dysentery, scabies. For these reasons the disease appears by predilection amongst the poorer portions of the population, who are most exposed to the effects of bodily labours and deprivations, as in the case of beggars, labourers, soldiers and sailors. On the same grounds it is the natives that are mostly attacked, whereas Europeans suffer far more rarely and only under special conditions such as occur in campaigns.

According to Brault, Arabs and Kabyles—in whom also phagedænic chancre and buboes occur—are particularly predisposed.

The disease more especially attacks men of middle age, a fact that is explained by such men having to expose themselves to the above-mentioned incidental causes.

SYMPTOMATOLOGY.

Injuries of the skin that are as a rule quite insignificant, usually form the point of departure of the disease. Such are excoriations of the skin caused by the shoes or sandals, superficial contused wounds, small

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lacerated wounds, such as may be got on the feet and legs through walking barefooted on sharp stones or thorns ; the stings and bites of insects ; eruptions in which there is a solution of continuity of the epidermis, as for instance, eczema, syphilitic and other ulcers originating from endemic boils.

According to Bechtinger the disease may also develop independently of cutaneous injury, commencing as little blisters that rise on the uninjured skin and burst after from twelve to thirty-six hours' existence.

Taking into consideration that phagedæna often occurs after slight contused and lacerated wounds, &c., in those predisposed by a low state of health, it is the more remarkable that in the *tropics* even large and serious *wounds* in the coloured natives usually *heal* very quickly and easily if kept clean. In white people also the healing of wounds is more favourable and less liable to complication than in Europe. The large amount of sunshine in the tropics perhaps acts as a bactericide, at all events it possesses desiccating properties. According to Ashmead the healing of wounds is very favourable in the American prairies which are distinguished by dryness of atmosphere (*Janus*, i., 1897, p. 515).

The *lower extremities* are usually the *seat* of disease, especially the dorsum of the foot and the shin, no doubt owing to the fact that these parts are most exposed to injury. More rarely the thigh is attacked, and more rarely still the scrotum and the upper extremity, especially the hand and forearm.

Sometimes the same individual is attacked by the disease on several parts of his body.

Sloughing phagedæna presents an ulcerative surface spreading by necrotic disintegration of the elementary tissues. The surface of the ulcer is covered by unhealthy granulations, covered by stinking pus and sloughs, or with a greyish pseudo-membrane adhering to the tissues below. The edges of the ulcer are irregular and undermined ; the surrounding skin has a bluish tinge, but is not swollen to any great extent. The ulcers exude a copious secretion and bleed easily ; the slightest blow, even a touch, suffices to cause at times considerable hæmorrhage. They rapidly extend, not only along the surface so that they cover the entire leg and sometimes the entire lower extremity, but they also extend in depth, muscles, tendons and bones being laid bare and necrosed. Sometimes large cavities filled with a foul greenish mass and swarming with maggots are found, in which pieces of gangrenous muscles, green-coloured shreds of nerves and tendons appear. Articulations are also sometimes opened and the small bones of the tarsus or metatarsus, or even entire toes, are shed. Arteries also may be opened, causing dangerous or even fatal hæmorrhage.

The exceeding painfulness of the diseased parts, the sleeplessness caused by such pain, with the drain on the system from the discharge, combine to reduce the strength of the patients more and more; they become cachectic, septic fever and diarrhœa set in, and death may ensue from exhaustion or septicæmia.

In other patients—and this is more frequently the case—the necrotic process stops short, sometimes suddenly, without any perceptible reason, the dead tissue is cast off, healthy granulations shoot up, the ulcerative cavity is filled up and after weeks and months cicatrisation sets in, or the atonic phagedænic ulcer is transformed into an ordinary chronic ulceration.

Sometimes more or less considerable deformities and mutilations are left ; toes are lost, anchylosis and contractures may form in consequence

PHAGEDÆNA OF WARM COUNTRIES.
Illustration by Dr. LE DANTEC. Reproduced from " Archives de Médicine Navale," by kind permission
of Dr. Bonnafy, Médicin en chef de la Marine.

of the cicatricial contractions, the long period of inactivity may lead to muscular atrophy, and so on.

According to Blaise *relapses* induced by attacks of fever are frequent.

Treille differentiates two distinct *forms of the disease*, a mild and a severe.

TREATMENT.

The first desideratum is to establish, if possible, a better state of the general health by nourishing food, wine, quinine and iron. Should syphilis be present the use of specific remedies, especially iodide of potassium, is indicated.

Local treatment is best *begun by thoroughly scraping out the base of the ulcer with the sharp spoon*, or to arrest the spread of the disease by destroying the surface and margins of the ulcer with caustics (fuming nitric acid, chloride of zinc, hydrochloric acid, &c.), or with the actual cautery whilst the patient is anæsthetised. According to Dempwolff, after scraping the ulcer, dressings consisting of cotton wool steeped in boiled water, lint, and a flannel bandage are applied, till such time as a non-suppurating, pink, granulating surface is formed. Occasional applications of caustic should be combined with this treatment.

Manson advises the use of pure carbolic for cauterisation ; and after its application, continued irrigation with a tepid antiseptic solution, followed by antiseptic dressings. Should the necrotic process, nevertheless, not be arrested, cauterisation must be repeated.

Fontan's treatment consisted in applying a 5 per cent. carbolic solution to the ulcers once or twice daily, and left on for an hour, or an hour and a half ; in the interval the ulcers were dressed with compresses smeared with boric-vaseline ; this observer found that good results followed his treatment.

The results attained by means of Stoker's oxygen treatment of chronic ulcers should encourage observers to give it a trial in tropical phagedæna. The treatment consists in a mixture of oxygen and air being made to act on ulcers by means of a special apparatus.[1]

When the phagedænic ulcer has been transformed into a granulating ulcer, the treatment of ordinary ulcers of the legs is adopted.

In order to accelerate cicatrisation, Plehn recommends that instead of skin-grafting according to Thiersch's method, by means of which he seldom attained satisfactory results, the skin on either side of the ulcer should be raised and brought together over the ulcerated surface. The deficiency caused by the displacement of the loosened flaps of skin from their normal position is remedied by skin-grafting from the upper arm and thigh. According to Plehn's experience the result in these cases where healthy tissue is grafted on healthy tissue, appears to be far more favourable and lasting than grafting of pieces of skin on the ulcer itself, be they ever so well prepared.

If the patients are much reduced in strength and the ulceration so extensive that there can be no hope of healing it, *amputation* of the affected limb is indicated.

Change of climate is supposed to exercise a favourable influence on the course of disease.

On the premises that phagedæna is contagious, the patients should be isolated, great care being taken that they by no chance come into contact with persons suffering from wounds ; their linen should be disinfected and disused bandages burned.

[1] E. Pfeiffer. *Korr.-Bl. d. Allg. ärztl. Vereins. v Thür.*, 1898, No. 8.

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VIII.

HYPERTROPHY OF THE EAR IN NEPAUL.

THIS peculiar affection mentioned by Hirsch was described by Campbell and Bramley as "Pendulous tumour of the ear," more than sixty years ago, and according to these authors this disease rages endemically in a very circumscribed district of Northern India, in the village of Nilkantha in Nepaul.

The *etiology* of the ailment is *unknown*. The natives blame the drinking water as the cause of disease, and Campbell frequently observed the condition to occur in conjunction with bronchocele. Bramley, however, denies any etiological connection between goitre and hypertrophy of the ear. The disease is more frequent in women than in men.

The disease commences as a small, firm enlargement, which is elastic to the touch, appearing on the outer aspect of the auricle; it grows quickly, and in one or two months attains the size of a pigeon's egg. It has a broad base, and is but slightly movable, as it is adherent to the subcutaneous connective tissue. Apart from the disfigurement it occasions no disorders; it is only when its growth is very rapid that the patients complain of a sensation of painful tension in the tumour. In such cases the skin over it exhibits a bluish discolouration and dilated vessels. If the tumour is punctured a thick whitish fluid exudes. The tumour may attain the size of an orange, or even that of a child's head, so that it sometimes hangs as low as the shoulder of the patient. At last, however, the contents soften and become absorbed, the skin shrivels and a thickened unsightly mass is left on the ear.

The disease generally appears on both ears, and usually several tumours develop on the same patient, one after the other.

To my knowledge there are no recent publications respecting this disease.

The *negroes of the Loango Coast* are subject to *lipoma of the lobe of the ear* (often on both ears). These enlargements may become the size of a walnut, or even a child's head, and may probably be attributed to the fact that the negroes pierce the lobes of their ears with thorns or sharp pieces of the ribs of oil palm leaves, and habitually wear these foreign bodies in the ears. (Falkenstein, *Virch. Arch.* 1877, lxxi., No. 4, p. 433.)

For keloids of the ear see p. 580.

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IX.

GOUNDOU.

On the West Coast of Africa there occurs endemically a peculiar form of nasal swelling called *goundou and anàkhré* that is, big nose, in the Agni language; on the Gold Coast the disease is called *henpuye, i.e.,* dog nose.

The disease appears to have been first observed by MacAlister (1882) and Lamprey (1887), for the "horned men in Africa," described by these authors, were undoubtedly persons afflicted with this ailment. We are, however, indebted to Maclaud for the first detailed communications in regard to it.

Hitherto we know the Gold, Ivory and Sierra Leone Coasts to be the geographical region of distribution of this disease. In a few districts it is fairly common; on the lower banks of the Comoë (Ivory Coast) there is about one case to every hundred of the inhabitants. The disease is not confined to any particular tribe of negroes and probably also occurs in West Indian negroes. Strachan observed a swelling similar to goundou in a West Indian negro child, but this was said to be congenital.

The disease usually commences during the latter years of childhood. Small bony excrescences about the size of a bean develop symmetrically on both sides of the nose, rarely on one side only; they apparently proceed from the nasal process of the superior maxilla, and mostly grow slowly but continuously and more or less evenly on both sides. When the patients have attained the age of fifteen years the tumours are usually the size of an almond; by the twentieth year they are the size of pigeons' eggs, by the thirtieth year they are the size of a hen's egg. The largest tumour which Maclaud observed, in a man between sixty and sixty-five years of age, was as large as an ostrich's egg.

The tumours (see table vii., fig. 57) are of an oval shape; their long axis is directed from above downwards and outwards. They are sharply circumscribed, smooth, immovable, as hard as bone, insensitive to the touch and are connected with the nasal bones and nasal processes of the superior maxillæ. The skin over them is normal and movable.

According to Chalmers they consist of a spongy bony substance, covered by a thin shell of compact bone, and are the product of an *osteoplastic* periostitis.[1]

The tumour pressing inward encroaches upon the nasal cavities; in other respects, however, the nasal passages are normal; the same holds good in regard to the oral and orbital cavities.

At the commencement of the disease the patients sometimes complain

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[1] They are thus distinctive in structure from Virchow's *Leontiasis ossea,* in which the bones are usually of a remarkably firm texture, resembling ivory in appearance and ardness.

PLATE VII.
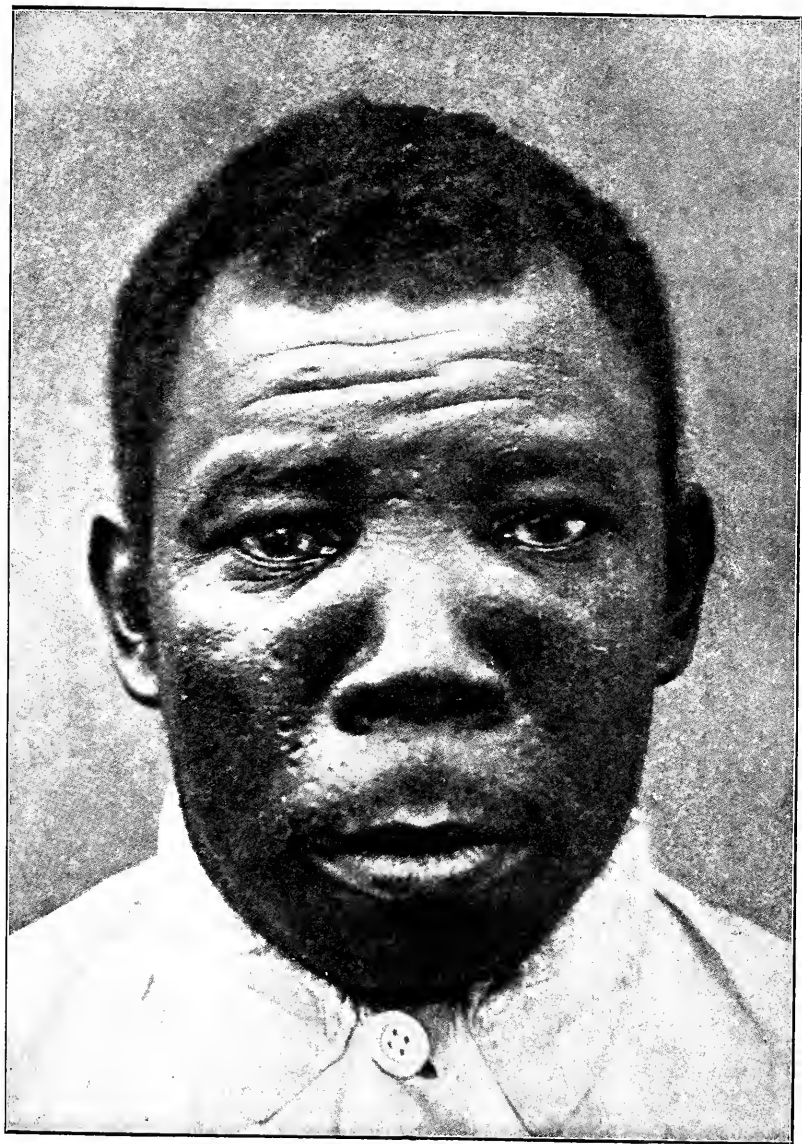
Fig. 57.
NEGRO FROM THE COAST OF SIERRA LEONE WITH GOUNDOU.
From a photograph by Dr. W. RENNER.

of severe pains in the head, these, however, cease after six months or a year. The later course of the disease is almost quite painless. Chalmers mentions that pains occur in the bony growth in wet weather. At first, also, there is frequent bleeding from the nose and muco-purulent or sanguino-purulent rhinorrhœa.

When the tumours have attained considerable dimensions they obscure the line of vision, and cause the patients to squint; atrophy of the eyeball occurred in a case recorded by Maclaud.

No further discomfort, apart from the disfigurement, are induced by the disease, which persists for many years. No signs of inflammation are observed in the tumours.

The *etiology* of the disease, which is supposed also to affect monkeys, is obscure. Maclaud is inclined to attribute the disease to parasites—the larvæ of dipteræ—which have penetrated through the noses of children; later observations, however, annul this view.

Chalmers seeks to connect this disease with frambœsia; he observed that the tumours always developed during or soon after that ailment.

The affection is not hereditary. It is observed more frequently in men than in women.

In regard to *treatment*, removal of the tumour is the only expedient.

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X.

MADURA FOOT.

DEFINITION.

THIS is a disease that occurs principally in India ; it is usually situated in the foot, and is originated by vegetable parasites. Madura foot is characterised by an unshapely tuberculated swelling, with cysts containing the parasites, and permeated with fistulous tracts.

NAMES.

The disease is called *Padaralmicum* in Sanskrit,[1] *Perical* or *Anaical* in Tamil,[1] *Slipada* in Bengal,[1] *Hatty-ka-Pung* in Deccan, designations that signify "large foot" or "elephant foot"; *Kirina-grah*, "dwelling of worms," is its name in Rajputana, and Gutlu madhe, "egg foot," in Bellary.

The following are the scientific names given to the disease by European doctors: Madura Fuss, Fungus disease of India, Fungus-foot disease of India, Madura disease, Mycetoma, Morbus tuberculosus pedis, Ulcus grave, Podelkoma, &c.

HISTORY.

Kämpfer (1712) was the first European doctor who mentioned this disease under the term *Perical;* and the disease was discussed in Benj. Heyne's historical and statistical news of India of 1806. It was, however, always confused with elephantiasis. The first indications that Madura foot is a specific disease is furnished in Brett's Surgery of India (1840), and in the military-medical reports from the Presidency of Madras, by Godefrey and Colebrook (1850). Ballingal (1855) and Eyre (1860) gave the first detailed descriptions of the disease, but Vandyke Carter has gained the greatest distinction through his researches regarding this disease.

GEOGRAPHICAL DISTRIBUTION.

It was believed until recently that Madura foot only occurred in India, or in persons coming from thence. Lately, however, cases of this disease have also been observed in Senegambia (Bérenger-Féraud,[2] Duval,[2] Carpot,[2] Le Dantec); Algiers (Gémy and Vincent, Legrain); North America (Kemper,[3] Adami and Kirkpatrick, Hyde and Senn[4]); Chili (Layet[3]); and Italy (Bassini and Campana), so that its region of distribution appears to be considerably larger. F. Plehn observed three cases in Suahelinese on the Tanga coast, which, however, had probably been carried thence from India.

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[1] Indian vernaculars.   [2] According to Le Dantec.   [3] According to Vincent.
[4] Delbanco, on the grounds of the material sent to him for examination by Hyde and Senn, believes that their case was not one of Madura foot, but one of actinomycosis.

In India it is the *Presidency of Madras* in particular in which Madura foot is endemic, and there it is found in Bellary, Guntur, Cuddapah, Pondicherry, Combaconum, Karrikall, Tanjore, Trichinopoli and other places. In the *Presidency of Bombay* the disease occurs on the declivities of the Western Ghauts, in Ratnagiri, Poona, Kattywar, Gujerat, Cutch, Karachi and Sinde. It is less frequent in the *Bengal Presidency*, but is observed in Bikaneer, Bahawalpore, and other districts of Rajputana, in Delhi, Hissar, Jhelam (in the Punjab) and in Bengal. I saw an Indian with Madura foot in Colombo, Ceylon.

SYMPTOMS.

One of the feet, usually the right, is the most frequent *seat of the disease*, but sometimes also the hand is affected. Occasionally it is confined to one toe, or one finger. In rare cases the leg may be attacked, the disease proceeding from the foot to the ankle and thence to the leg. In a case recently published by Keith Hatch and Childe, the disease was situated in the region of the knee, the foot not being affected. Other parts of the body are only exceptionally attacked. Maitland once observed the disease on the thigh and abdominal wall. Smith saw it once on the neck. According to Collas *Epulis gravis*, the *pseudo-cancer* of the inferior maxilla, which is observed in Pondicherry, is identical with this disease. It is exceedingly rare to find the simultaneous occurrence of the disease on different parts of the body.

It is very seldom that medical men have the opportunity of observing the disease at its very commencement, for the natives only present themselves for treatment when the disease has made considerable inroads. The disease begins with the development of one or several small hard *nodules* in the subcutaneous tissue, which are painless or only sensitive on being touched, and which grow slowly. Carter states that he has observed as an initial sign, preceding the appearance of the nodules, reddish lines in the depth of the skin.

The first nodules are usually situated on the sole of the foot, but they may appear on the instep, or between the toes. After several months they come to a head, burst and discharge the contents (to be described below) through fistulous openings.

In the meantime fresh nodules continue to form and the circumference of the foot gradually increases so that it is sometimes two or three times its normal size. Its shape likewise has changed. The arch of the foot has disappeared and instead of being concave it is convex. The sides of the foot have become rounded and the normal bony prominences are obliterated by the swelling. The shape of the foot, in consequence of these changes, has become more or less cylindrical or oval. The toes are pushed far apart, or deviate from their normal position in other ways, and on account of the convexity of the sole they can no longer touch the ground. The nails generally are intact.

The surface of the foot is studded with *prominences* and *nodules* which vary in size from a pea to a small cob-nut and which are of a hemispherical, more or less symmetrical, shape. Sometimes they are distinctly outlined, sometimes more diffuse, part of them hard, insensitive and covered by normal skin, part of them dark red, soft, fluctuating and sensitive to touch.

Between the prominences and nodules there are numerous warty, raised, or funnel-shaped *openings*, surrounded and partly covered by pale red granulations which are not sensitive and do not bleed readily ; these

are the result of the perforation of nodules. The probe may be passed through these openings into sinuous fistulous tracts, more or less deeply, into the interior of the foot, and may even penetrate into the bones. If the disease is far advanced the probe nowhere meets with resistance, but easily penetrates the softened caseous mass in all directions. There is but little hæmorrhage even on probing.

There exudes from the openings a thin, sanious, dirty white or yellowish, syrup-like or oily, stinking *liquid*, which is sometimes streaked with blood, and in which numerous small bodies, to be described later, are suspended. The microscopical examination of this exudation exhibits numerous drops of fat, crystals of fatty acids, finely granulated detritus, elements of connective tissue and isolated white and red blood corpuscles.

The peculiar *cellular bodies* contained in this liquid, are sometimes of a grey or yellowish and sometimes of a blackish colour, and on this account *white* or *pale* (*ochroid*), and *black* (*melanoid*) *varieties* of the disease are recognised ; in rare cases (Lewis and Cunningham) both kinds appear side by side in the same patient.

The bodies of the *pale variety*, which are reminiscent of the spawn of fishes, vary in size from a pin's head to a pea and even larger ; the smaller bodies are of a round or oval shape, the larger have an irregular outline and are grey, yellowish or reddish in colour and of a soft dough-like consistency ; these bodies are not soluble in ether, potash or acetic acid, which controverts Lewis and Cunningham's assertion that they are of a fatty nature.

In the *black variety* the bodies vary in colour from brown to black (Bristowe's truffle-shaped bodies) and they resemble grains of coarse gunpowder. Their size and shape is similar to that of the white variety ; they are, however, of firmer consistency, but nevertheless can be broken up.

The microscopical examination of these little bodies shows that they consist of fungoid elements.

According to Thudichum's spectroscopic researches, the black bodies contain no hæmoglobin in any form, and are not soluble in either potash or diluted or concentrated sulphuric acid ; after being burned a small quantity of ash is left which contains a little oxide of iron, but far less than if a proportionate quantity of altered blood had been burned ; the black colour, therefore, has nothing to do with blood.

According to Le Dantec, the bodies are soluble in hot sulphuric acid, the liquid becoming yellowish red ; according to Boyce and Surveyor they are decolourised by hypobromite of soda ; on the other hand the colour does not disappear with alcohol or chloroform (Lewis and Cunningham).

The quantity of liquid exuding from the openings appears to be different in different patients, it seems to decrease with rest and increase with motion. If the secretion is slight, the fluid dries up on the granulations in thin eschars, which are easily loosened and shed when the flow is increased.

In a case observed by Shattock (*Brit. Med. Journ.*, 1898, March 5, p. 622) the skin exhibited a peculiar and pronounced papillomatous condition. The coarse papillary processes which partly again carried secondary papillæ, contained cysts filled with masses of fungi. Shattock designated this form of disease *Mycetoma papillomatosum.*

On palpation the diseased foot communicates a sensation of elasticity, or as if one were pressing on a thin sheet of metal. Impressions with the fingers leave no pits.

Sensibility is maintained. There is, as a rule, no *pain* at all. Sometimes the patients complain of a dull sensation of pain on pressure. Exceptionally cutting or shooting pains are observed extending to beyond the knee. In one of Legrain's patients the leg was very sensitive to cold ; and in winter and in damp weather pains developed in the leg.

The great unshapely foot forms a strange contrast with the emaciated leg, consisting almost only of skin and bone. Collas found that the inguinal glands of the diseased side were much enlarged, but painless. In exceptional cases other lymphatic glands become affected.

Locomotion is hindered by the swollen foot, and later on the patients become quite incapable of walking at all.

The *general health* and the *condition of nutrition* remain undisturbed for a considerable time. When at last, after the course of years, the patients suffer from anæmia and cachexia, the condition is less attributable to the disease itself than to the misery and want to which the sufferers —mostly belonging to the lowest classes of population—are reduced, in consequence of their inability to earn a living.

The disease has a very *chronic course.* There is no tendency to heal. Although it may happen that a few nodules disappear, and a few fistulous tracts close and heal, leaving cicatrices that are first white and later on pigmented and radiated, the disease systematically advances. If left to itself, *i.e.*, without operative interference, the patients at last perish from exhaustion, diarrhœa or other intercurrent diseases; nevertheless, the disease, from its commencement to the death of the sufferer, may persist from ten to twenty years.

PATHOLOGICAL ANATOMY.

When an incision is made through a foot or any other part of the body in which the disease is fully developed, it will be seen that beneath the thickened skin all tissues, the connective tissue as well as the muscles and bones, are transformed into a similar viscid, jelly-like mass of a grey or reddish colour, so that the knife can be pushed through in every direction without encountering much resistance. The jelly-like mass is permeated by numerous spherical cysts of various sizes, and from these again there lead sinuous canals, some of which have a blind termination and some of which open out through the skin. The cysts, as well as the sinuses, are filled with peculiar masses of fungi, sometimes of a grey or yellowish, sometimes of a brown or black colour; they are usually designated mulberry-shaped bodies, and are of a doughy consistency. Examined more minutely, they are found to consist of agglomerations of the bodies described above, which exude through the fistulous openings. After the removal of the masses of fungi the cysts and sinuses are found to be lined by a membrane, consisting of granulations, which, when found in bones, is easily separated, but which is more adherent to the soft parts.

This disease therefore is undoubtedly attributable to an *invasion of vegetable parasites*, which disintegrate and transform the tissues of the affected part. The connective and adipose tissues around are transposed into a condition of chronic inflammation, which leads to a neoplasm of connective tissue. The adventitia of the vessels becomes thickened. The muscles, according to Corre, suffer a glassy-like metamorphosis of their fibres; they lose their transverse striæ, and breaking up into *débris* finally disappear altogether. Liquefaction takes place also in the carti-lages. When the bones become affected, the traces of a chronic periostitis and its consequences are exhibited at first. In a later stage softening and atrophy of the compact tissue sets in, and honeycomb-like cavities, crammed with the parasites, form in the cancellous tissue. Never, or but very rarely, however, do the bones become carious. The smaller bones

may vanish entirely. The tendons and aponeuroses possess the greatest power of resistance against the parasitical invasion, and therefore remain almost intact.

In the case recorded by Keith Hatch and Childe, in which the region of the knee was affected, the bones, apart from slight osteophitic formation at the internal condyle of the femur, were not attacked. On the other hand, the inguinal and femoral glands on the affected side, and the glands along the femoral artery, as well as a few mesenteric glands, were enlarged and exhibited a reddish-brown colouration probably attributable to hæmoglobin. Besides this condition, masses of fungi of the size of hemp-seed and of a yellowish colour, were found in the inguinal and femoral glands.

We are in possession of valuable information of the *microscopical structure of Madura foot*, through researches made by Kanthack ; this author kindly sent me preparations, by means of which Unna and I were able to confirm his observations.
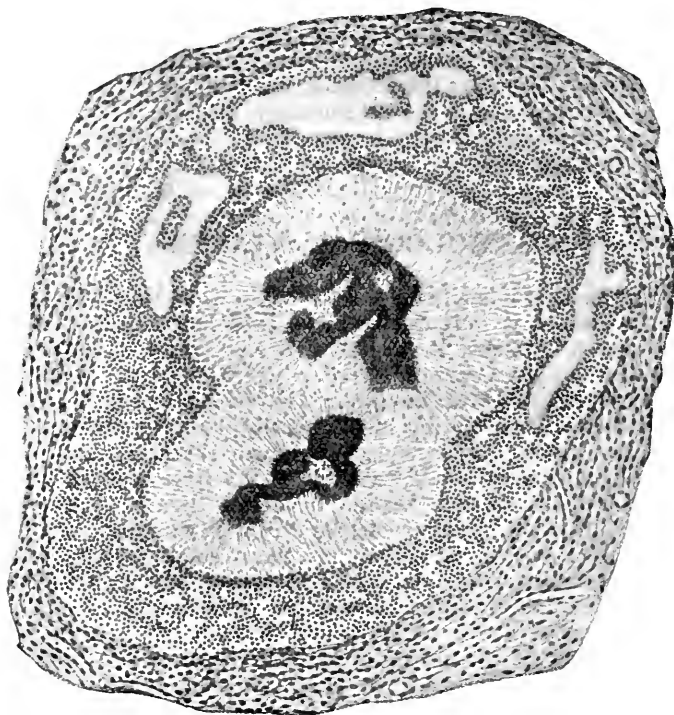
FIG. 58.—Madura foot. Two fungoid glands surrounded by a zone of suppuration and fibrous granulation tissue.—Zeiss, Obj. D., Oc. 2.

Kanthack differentiates three stages of disease in the *white variety*. In the *first stage* there is an agglomeration of round cells at the circumference of the fungoid glands. In the *second stage* the fungoid glands are surrounded by granulation tissue with epitheloid and hyaline cells (Unna), the latter appearing as deeply coloured, glittering spheres which are partly closed up in cells, partly free. Here and there the fungoid glands are seen to be surrounded also by giant cells and dilated blood-vessels, the endothelium of which is distinctly proliferated, while the fungoid mass exhibits signs of degeneration consisting of a radiating hyaline infiltration. In the *third stage* (see fig. 58) the degeneration is still further advanced, the granulation tissue is partly transformed into fibrous tissue, and slight suppuration develops around the separate fungoid glands, leading to the formation of abscesses and fistulæ which rupture the one into the other, or break through the surface.

Each of these cavities exhibits a fibrous, often pigmented, ring on the outer aspect,

in which granulation tissue develops with a zone of leucocytes, and closely surround the fungoid granular detritus. The fungoid glands are either isolated or agglomerated. When isolated they are of a crescent or kidney-shape, when agglomerated mulberry-shaped. They consist of a plexus of mycelium which at its periphery is closely ramified, but at its centre is only loosely adherent, and from which, radiating outwardly like the ribs of a fan, are to be seen closely pressed, large, transparent, glittering prisms or columns, which are difficult to stain and along which, when stained, fungoid fibres can be traced. These prisms do not represent organs of fructification, but products of degeneration, and are most strongly developed where the fungus is closely shut in by fibrous tissue. The radiating tracts do not entirely surround the fungoid gland, for at one part the radiation as well as the close marginal zone is missing, and at this place the mycelium grows towards the periphery in a stem-like manner. The fungus filaments are thin and solid and usually exhibit no interruptions but actual ramifications; in Adami and Kirkpatrick's case a part of the hyphæ, however, exhibited transverse divisions. In the later stages there are deposits of pigment in the fungoid filaments.

The *black variety* of the disease presents a different aspect. In cases of long standing, according to Kanthack, only brown and black scales of pigment of various sizes are found without a trace of mycelium. Cases of more recent standing exhibit reddish or yellowish-brown masses shading into black, which are formed of an entangled network of broad, hollow, varicose filaments which radiate from a centre and terminate at the periphery in small clubs. In between these are round bodies which evidently represent sections of filaments. In fresh cases—in one of the three cases examined by Kanthack—a peripheral zone of glassy, homogeneous rays may be distinguished in which, in coloured preparations, mycelium threads with club-like terminations may be traced. Conjoined to this zone there is a mycelium net which is closer towards its edges than its interior, and the marginal zone of which is pigmented. The pigment is situated in the filaments, which are broad, varicose, and often interrupted, having the appearance of chains of rodlets; others, however, appear to be hollow. In this case every transition was found from the youngest stage similiar to the pale variety, to the brown or black masses without mycelium. The old forms are found in firm fibrous tissue, the recent ones, on the other hand, in liquefied suppurating tissue.

Delafield's hæmatoxylin and watery eosin or methylene blue will be found most suitable for staining Madura foot preparations.

In a few cases (Lewis and Cunningham) no masses of fungi were found in the cysts and sinuses, which only contained a purulent oily material.

ETIOLOGY.

As already observed, Madura foot is originated by *vegetable parasites*. Ballingal was the first to recognise the parasitic character of the disease; Vandyke Carter was the most energetic champion of this view, and it was he who gave the disease the designation *mycetoma*. Berkeley also succeeded in cultivating a hitherto unknown fungus from a preparation sent to him by Carter, and to which out of compliment he gave the name *chionyphe Carteri*. He himself, however, subsequently denied its etiological signification.

After the discovery of actinomycosis in Europe, Carter was the first to point out the similarity of the two diseases, and Hewlett and others even declared them to be identical.

This view, however, is contravened on radically important grounds. I need only recall the different size and colouring of the fungoid masses in the two diseases, their different localisation, and the difference of their course, which in Madura foot is more benign and more chronic than in actinomycosis. The pronounced tendency also for actinomycosis to spread to other near or distant parts of the body, to attack the internal organs, and the transmissibility of actinomycosis to healthy persons, are qualities which, at least according to our present knowledge, are not possessed by Madura foot. Moreover, the hyphomycetes of Madura foot are more delicate, stain remarkably well with hæmotoxylin, showing the prisms and columns described above as staining with difficulty. Actino-

myces, on the other hand, is not stainable with hæmotoxylin and develops clubs and knobs which are difficult to stain.   Recently, also, Vincent, by means of pure cultures, has furnished proofs—at least as regards the white variety—that the masses of fungi found in Madura foot do not belong to the actinomyces, but to a species of streptothrix designated *streptothrix maduræ*, by this observer.

Kanthack had previously declared that the parasite appertained to the class of *streptothrix* (Cohn) or *oospora* (Wallroth), and suggested the name *oospora indica* for it, whereas Nocard and Blanchard designate it *discomyces Maduræ*.

The material used by Vincent for the preparation of cultures was taken by him direct from the diseased tissue with the usual antiseptic precautions.   It exhibited but little growth in bouillon, but infusions of hay and straw (15 g. to 1 litre, and not neutralised, and therefore with an acid reaction) were found to be suitable nutritive media.   The same holds good for meat soups, to which yellow turnips, carrots, and more especially potatoes (20 g. to 1 litre) have been added, after previous filtration and sterilisation.   The temperature should be about 37°.   The growth stops at a heat over 40°.   The cultures, which are placed in wide tubes or Erlen-Meyer's bulbs, to which air is accessible, exhibit small grey flakes, round or flat, on the fourth or fifth day ; they cling to the walls and bottom of the tubes, and after from twenty to thirty days attain the dimensions of a small pea.   Some of the flakes exhibit a brown tinge in the centre, while others that lie near the surface of the liquid become pink or red after a month or two.   The nutritive fluid never becomes cloudy, for most of the flakes lie at the bottom, where they form a covering which exceeds $\frac{1}{2}$ to 1 cm. in thickness.   The nutritive fluid, previously acid, in time assumes an alkaline reaction, and becomes pale blue.

In ordinary gelatine the streptothrix maduræ only exhibits a weak growth of white colonies along the inoculative puncture on the surface.   Vincent considers that 100 ccm. of an infusion of hay or potatoes, with the addition of 6 g. gelatine, 4 g. glycerine, and 4 g. glucose, neutralised and sterilised in the usual manner, to be the best solid nutritive soil.   The streptothrix does not liquefy the gelatine.   On this soil fine luxuriant round glazed colonies of a white or pale yellow colour are obtained, which later on often assume a pink or even red colour.   If very many colonies form on the gelatine they remain small, but if fewer in number are present they attain almost the size of a pea.   They then resemble an inoculation pustule sunk in the middle, and of a white colour, the margins assuming a red tint.   Old cultures fade and become sickly white.   The colonies are of a horny consistency, and cling very firmly to the nutritive medium.

The parasite grows fairly well on milk without coagulating it, though it becomes slowly peptonised.   On eggs and serum, however, it does not flourish at all.

On potatoes, from the fifth day, and at 37°, small, uncoloured, or whitish prominences are seen, which assume a pale reddish colour after a month.   This gradually deepens and becomes sometimes a bright pink, sometimes orange-colour or red, sometimes a fine dark red.   This occurs particularly when the potatoes have a strong acid reaction, whereas on some potatoes there is no colouring at all.

Some colonies are covered by a fine white dust which consists of spores.

The parasite is aerobic.   The parasite stains well with basic aniline stains, more faintly with safranin and eosin.   It can also be stained according to the methods of Gram and Weigert.   A solution of iodine stains it yellowish-brown, while hæmatoxylin causes it to assume a violet colour.

The fungoid filaments are finer in the cultures than in the little bodies described above ; their breadth does not exceed 1 μ.   The irregular swellings and contraction observed in the little bodies are not observed in the cultures, which, however, when two weeks old often exhibit a series of *spores* at the end of the filaments.   They are ovoid, light refracting and about 1·5 μ in breadth and 2 μ in length.   They stain well with aniline dye and according to Gram's method.   They exhibit very little resistance to heat ; they are killed in three minutes at 85°, and in five minutes at 75°.   The cultures that do not carry spores die in three to five minutes at 60°.

The formation of spores takes place best where the mycelium comes into contact with the air, and this is the case in fluid nutritive media as well as on potato.   Cultures with hay-broth are the most suitable for this purpose.

One may actually see the spores develop in fresh broth and in suspended drops.

The cultures are very resistant to desiccation ; even after a period of twenty-one months they exhibited a capacity for development.

The streptothrix Maduræ does not prove pathogenic to animals (rabbits, guinea

pigs, mice, cats). Bocarro's experimental transmissions with fresh material of both varieties were negative in rabbits as well as in dogs.

By means of parallel cultures arranged and kept under exactly the same conditions, Vincent confirmed the difference between the streptothrix Maduræ and the actinomyces, as shown on the table.

Boyce and Surveyor likewise succeeded in culturing a *streptothrix* in a case of the *white variety;* it exhibited a condition similar to that cultivated by Vincent, but no ramifications and spores could be discovered.

Legrain could not cultivate colonies in infusions of hay, but succeeded in doing so on gelatine with malt and peptone. The colonies were round, prominent, glazed, very adherent to the lower surface, at first pale, then golden-yellow, and soon after became of a vivid red colour and finally became decolourised.

In the nodules which exhibited *suppurative degeneration,* Vincent found *staphylococcus pyogenes albus* and *aureus* in addition to the parasites described.

In the *black variety* it is either the question of a degenerative form of the pale variety or of some other variety of the same fungus. Kanthack, as the result of his researches mentioned above, is inclined to the former view. Possibly the differences of colour exhibited by the pale variety is caused by different kinds of fungi. Madura foot, probably like actinomycosis, and trichophytosis, is not a clinical entity, but a complexity of diseases not yet sharply differentiated one from the other of which each has its particular cause. Hitherto Le Dantec has been the only investigator who has succeeded in obtaining cultures of the black variety. His discovery, however, does not coincide with the results of the microscopical investigations, so that we have to await confirmation of his discovery.

No.	Cultures or Inoculations	Streptothrix Maduræ	Actinomyces
1 ..	Peptonised beef tea ..	Moderate growth	Luxuriant growth.
2 ..	Sterilised infusion of hay or straw	Principal nutritive soil; growth rapid (four days) and luxuriant	No growth.
3 ..	Ordinary peptone-gelatine	Does not liquefy	Liquefies.
4 ..	Gelatine with infusion of hay	Very quick growth; the culture becomes pink or red on the surface	Whitish, very weak culture.
5 ..	Glycerine gelatine ..	Colonies which at first are white, then pink or red, and provided with a sunk centre	At first white, later on greyish spots; folded.
6 ..	Potato	Bright pink, vivid or dark red culture; does not brown the substratum	Close, wart-like, yellow and white, black-edged colonies; potato becomes brown.
7 ..	Cabbage, yellow turnip, carrot	Growth	No growth.
8 ..	Serum	No growth	Growth.
9 ..	Egg	,, ,, ...	Growth.
10 ..	Cultures in areas deprived of air	,, ,, ...	Facultatively anaerobic.
11 ..	Inoculations	Not transferable to any animal	Transferable to rabbits, guinea pigs, calves.

Le Dantec cultured, from the truffle-shaped bodies obtained from a case from Senegambia, staphylococci and streptococci as well as short *bacilli,* the latter grew into long filaments in bouillon, but exhibited no ramification, real or false, at any period of their development; they were, therefore, not a species of streptothrix. Only after a previous culture in bouillon could cultivations be made on solid nutritive soils. Cultures

whether made in bouillon or on solid nutritive media, gradually become reddish, rust-coloured. Gelatine was liquefied by the bacilli. Experimental transmissions to rabbits and guinea pigs failed.

The origin of Madura foot, or of the parasite that generates the disease, is unknown.

It has been endeavoured to trace the cause of Madura foot to various soils, but without success ; it has been proved, however, that the disease has been observed in regions which, in so far as the sorts of soil and the species of flora incident to them is concerned, show great diversity. Its limited appearance, however, seems to point to the fact that the parasite is associated with certain local conditions. Probably the parasite is a saprophyte living on plants.

Racial peculiarities play no part in the etiology of Madura foot. The disease has been observed in persons of the most diverse races (Hindoos, Eurasians,[1] Kabyles, North Americans, Mestizoes, Italians, &c.).

The disease has not been observed in Europeans in India, whence the greatest number of the observations originate. Their immunity, however, is certainly less attributable to racial difference than to the more favourable *hygienic conditions* under which the whites live, and above all to the fact that they all *wear foot gear*. As to the natives, no caste, no class is spared ; the disease occurs in the Mussulman as well as in the actual Hindoo ; it is, however, most frequent *amongst the lowest classes of the population*, who live in miserable hygienic conditions, and amongst the *agricultural people*. In contradistinction to its frequency in the country it is very seldom seen in large towns, a circumstance which, according to Carter, is attributable to the improved hygienic conditions provided by the European residents.

Walking barefoot plays a prominent part in the genesis of this disease. This custom affords opportunity for *injuries* caused by stones, thorns (Bocarro often found thorns of the acacia arabica embedded in the swelling), prickly plants, &c., from which Hindoos notably suffer frequently. The invasion of the parasites may then take place through the injured skin, or the substance causing the injury may be the carrier of the infection. Carter considers that the sweat glands form the point of entrance for the parasites. The similarity of Madura foot to actinomycosis leads one to consider the possibility of injury by means of corn (bristles, &c.) beset with fungi piercing the skin. This would explain the frequent occurrence of the disease amongst the country folk, they being particularly exposed to such injuries.

Hogg reports a case which, in regard to its connection with an injury, is interesting. The patient, six months previous to his admission into hospital, struck his foot against a stone causing a deep incised wound which healed under the application of poultices and was forgotten. After a few months, however, a gnawing pain set in at the former seat of injury, reminding him sharply of the same. An abscess then formed there from which the characteristic little bodies exuded.

In the case observed by Bassini and Campana in an Italian agriculturist who had never left his native province, the disease occurred subsequent to an injury to his foot from a pitch fork. In Keith Hatch and Childe's case, which has been repeatedly mentioned, the outbreak of the disease had been preceded by a heavy fall on the affected knee.

In regard to *sex, males* are much more frequently attacked by the disease than females. Carter computes the proportion as about 10 : 1. In this connection, however, it must be remembered that Hindoo women,

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[1] Offspring of Europeans with Indian mothers.

in consequence of their usages and religion, seek medical treatment far less frequently than men (Corre).

The disease occurs most often during the prime of life, between the 20th and 45th year, very rarely earlier, somewhat more frequently in later years. It is unknown in childhood.

DIAGNOSIS.

The diagnosis of Madura foot presents no difficulties. It is easy to avoid confusing it with carcinoma, sarcoma, tuberculosis, syphilis, nodular leprosy or elephantiasis, and with dracontiasis and endemic Oriental sore. The differences between Madura foot and actinomycosis have been pointed out above.

PROGNOSIS.

The disease is incurable, but when an operation is performed in due time the prognosis, *quoad vitam,* is good.

PROPHYLAXIS.

As the disease in most cases may be traced back to injuries of the foot, it seems that the most practical method of avoiding it is the wearing of shoes or sandals. Moreover, care should be exercised to keep the feet clean.

TREATMENT.

The treatment of Madura foot is principally *surgical.* In the early stages of the disease cauterisation is indicated by means of the actual cautery. Paquelin's cautery, or escharotics, especially caustic potash, eradication by scraping, followed by injections of iodoform—glycerine—emulsion, have also been tried. In suitable cases extirpation of the nodules may be undertaken. In addition, interstitial injections of solution of chloride of zinc may be tried. If, however, the disease is already advanced, *amputation* is the only remedy left ; this gives a good prognosis, provided that all diseased parts are removed. Sometimes there is latent disease of the bones of the legs, therefore amputation must be made through the healthy tissues. Provided this is done a recurrence of the disease may be prevented. Collas has performed this operation in 126 cases, 117 successfully ; in only two cases did relapse occur.

Medical treatment in Madura foot is reckoned to be useless. Iodide of potassium, which in actinomycosis of man and beast has been used with favourable results, has proved to be inefficacious in Madura foot.

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XI.

AINHUM.

AINHUM is a disease that occurs principally in negroes, it affects single toes and is characterised by a ring-shaped constriction which finally leads to amputation.

NAMES.

The word ainhum originates from the negro-language, and signifies "to saw," because the stump left looks as if sawed off. In the Soudan the disease is called *Banko-kérendé*, in India *Sukha pakla* (*i.e.*, dry suppuration), in Brazil *Quigila*.

GEOGRAPHICAL DISTRIBUTION.

The disease has hitherto only been observed in the coloured races, principally in *negroes*. The *West Coast of Africa* forms its principal seat. Clarke (1860) was the first to report a " dry gangrene of the little toe among the natives of the Gold Coast." Moreover, cases are reported from the Soudan, Algiers, Egypt and the Northern part of the Transvaal. Next to Africa the largest number of cases of ainhum have been observed in Brazil, although latterly it is not so prevalent as formerly ; the reason for this being probably, as Da Silva mentions, attributable to the number of negroes having decreased there. The occurrence of isolated cases, particularly in negroes, has also been reported from Buenos Ayres, British Guiana, the Antilles, from a few States of North America, from the Islands of Madagascar, Nossi-Bé, and Réunion, from the Pine Island belonging to New Caledonia, and the Gilbert Islands.

Besides negroes, the disease has been principally seen in *Hindoos* in India. In Syria (Beyrout) De Brun observed two cases in persons of the *Semitic* race.

SYMPTOMS OF DISEASE.

One or both *little toes* are as a rule the *seat of the disease*. In the latter case the toes are either attacked simultaneously or one subsequent to the other. In one of Dupouy's cases almost twenty years elapsed between the disease of the two toes ; in one patient of Duhring's there was an interval of thirty years. The disease sometimes occurs to the fourth toe, but this is much more rare. Da Silva compiled fifty cases of ainhum, in forty-five of which the fifth toe, and in five of which the fourth toe was affected. Guimaráes twice observed ainhum on the fourth and fifth toes of the same foot ; Gongora saw the disease once on the second toe, and Cooper saw it once on the big toe. In one case of

De Brun's the five toes of the one foot were all attacked, but only the fifth toe of the other foot.

Guyot states that he observed the disease on the fingers also ; to me, however, it seems doubtful if these cases occurring in Pine Island and the Gilbert Islands were really related to ainhum.

The disease commences with a shallow deepening in the form of a groove developing on the lower surface of the toe in the vicinity of the digito-plantar fold. This gradually creeps round to the inner and dorsal surfaces, and at last to the external surface likewise ; the furrow simultaneously also deepens, so that a deep groove surrounds the limb, which appears as if tied round by a string.

The segmented portion of the toe swells to twice or three times its normal size, and mostly exhibits a smooth surface of natural colour and lipomatous consistency. In progressive segmentation the toe at last remains hanging by a thin stem, easily movable in all directions, like a shrivelled cherry or a small potato. The nail is turned outwards on account of the diseased limb acquiring a lateral position. The nails mostly remain intact, but in some cases they become misshapen (Weber) or atrophied, and at last disappear (Guimaráes).

The disease seldom causes pain at first and locomotion is not hindered. Later, especially when walking, violent pain sets in, so that, if the diseased part does not become torn off by some accidental force or drop off spontaneously, the patient is bound to resort to a surgical removal of the toe, an operation which is either undertaken by the patient himself or by a surgeon.

Sometimes small, foul-smelling ulcers develop in the groove.

If the part is cast off spontaneously a small wound remains which mostly cicatrises in a short time leaving a small roundish stump. In rare cases ulceration persists.

The constriction generally takes place at the first inter-phalangeal articulation, sometimes at the second joint, and occasionally even in the continuity of the first phalanx, so that after being spontaneously cast off, splinters of bone protrude from the wound and retard its cicatrisation.

In a series of cases *trophic, vasomotor, sensory* and *motor disturbances*, particularly of the affected lower limb, were observed, serving to demonstrate the presence of a nervous affection. Thus Collas and Da Silva Lima found the skin on the foot dry, coarse and black, or blacker than on the other parts of the body ; the epidermis appearing puckered. In one case observed by Corre on Nossi-Bé the hands were scaly, the palms discoloured to a milky tinge and slightly wrinkled ; the feet likewise exhibited desquamation, and the toes unaffected by the disease were swollen and unshapely. In one case of De Brun's the skin on the affected lower limb was thickened, and on the dorsum of the foot shrivelled ; there was desquamation on the sole, the growth of hair was increased, the muscles wasted, sensibility decreased, the plantar and patellar tendon reflexes obliterated, and locomotion somewhat difficult in consequence of the stiffness of the diseased leg. Moreover, the foot was thickened and shortened, its arch flattened and its temperature about 0·4—0·6° higher than that of the other side. Dalgetty observed keratosis on the palms of the hands and the soles of the feet.

Dupouy's cases always exhibited *pains in the loins* as an initial symptom ; and these pains were occasionally so severe that the patients could neither walk nor eat.

There is never any disorder of the general health.

The *course of the disease* is very slow. Usually several years elapse,

till the constriction of the part has advanced to such an extent that the patient resolves to have it removed ; it even takes much longer, from five to ten years and more, until the toe is cast off spontaneously.

Relapses very seldom set in after the removal of the diseased member. Gongora observed one case in which at first the middle and distal phalanges were cast off spontaneously ; the disease then developed anew on the stump and led to the casting off of the proximal phalanx.

PATHOLOGICAL ANATOMY.

The anatomical and histological examinations hitherto made of toes, some of them spontaneously cast off, and some of them surgically removed, have furnished no specific conditions.   All investigators coincide in the opinion that the constricting ring is formed of fibrous tissue, into which all other tissues are merged, and over which the epidermis is considerably thickened.   In the amputated part the epidermis also exhibits some slighter thickening, and the *subcutaneous adipose tissue is very strongly developed*, similar to that of lipoma, accounting for the swelling of the limb.   The bones have partly disappeared, being transformed into fibrous tissue, or their medullary spaces are enlarged at the cost of the bony tissue ; the medullary spaces are also not filled as in the normal with red marrow, but with fatty cells which are embedded in a relatively rich stroma of connective tissue.   The interphalangeal articulations are sometimes anchylosed their cartilage being transformed into fibrous tissue.

A few investigators such as Schüppel, Duhring and Eyles, were unable, on the other hand, to confirm the hyperplasia of the adipose tissue. Duhring, besides describing a thickening of the epidermis, found inflammatory changes of the skin which he characterised as " inflammatory œdema."

The papillæ of the corium were elongated and broadened, their capillaries dilated and serpiginous, and the peri-vascular spaces filled with red and white blood corpuscles. In the immediate vicinity of the vessels there were agglomerations of small round cells in the reticulum of the connective tissue of the corium.

The small arteries and capillaries were filled with blood, the veins were mostly empty.   The tunica media and adventitia of the larger arteries appeared thickened ; their endothelia were proliferated.   The lymphatic vessels were dilated, but mostly empty, the sebaceous glands atrophied and their convolutions surrounded by numerous adipose cells and agglomerations of lymph cells.   Wile also observed the same inflammatory changes, and, in addition, this observer found accumulation of cells, as also newly formed fresh connective tissue.

Eyles places the changes of the *epidermis* in the foreground, and regards it as primary.

The exceedingly hypertrophied stratum of the epidermis, according to this investigator, is formed of horny cells, under which there is a chromophile, irregular, but distinctly thickened layer.   On horizontal sections the interpapillary proliferations, which here and there form complete nests of cells, are distinctly recognisable, and the cells lying within them are in themselves so changed that many of them, in lieu of the nuclei, exhibit pigmentations and vacuoles.   The cutis and subcutaneous cellular tissues exhibit a fibrous hyperplasia.   The adventitia of the arteries is thickened, as is the intima to an even greater degree, so that there are often unmistakable obliterations of vessels.   The deep capillaries exhibit a hyaline change, their endothelia are considerably enlarged.   The membrana propria of the sebaceous gland is thickened, its glandular epithelium proliferated.   Eyles designates the above-mentioned changes of the bones as rarefying ostitis.

Further researches are required for the elucidation of the histology of ainhum.   In any case the old opinion that in this disease it is a question

primarily of neoplasms of contracting connective tissue at the place of constriction, and of proliferation of adipose tissue in the diseased toe itself in consequence of disturbed nutrition, is in my opinion quite exploded.

ETIOLOGY.

The *cause* of ainhum is up to the present quite obscure. Da Silva of opinion that *injuries to the toes* caused by going barefooted induce the disease, but this view is negatived by the fact that the ailment is also observed in free negroes who usually wear foot gear. Gongora asserts that the disease is the effect of sheer perversity in the patient, who ties a string tightly round the toe to *mutilate* himself. This statement is obviously incorrect and unconfirmed.

The *wearing of rings* on the toes is an equally groundless reason given for the cause of ainhum.

Various observers, especially Proust, connect the disease with *congenital spontaneous amputations and constrictions of the skin*, which come to pass during fœtal life through the constricting effect of amniotic filaments. These, however, are congenital and occur on various parts of the body ; they are not limited to the toes, are generally multiple and frequently occur simultaneously with other deformities ; they therefore differ essentially from ainhum.

Zambaco is the principal exponent of another view—that ainhum appertains to leprosy. This author says : " L'Aïnhum des nègres Nagos, est une léprose légère monosymptomatique, dactylienne podique, c'est-à-dire mutilante des pieds."

Mutilations, resembling ainhum, certainly do occur in leprosy in rare cases, as observed by Zambaco, v. Düring, Ehlers and others, but they mostly affect the fingers, rarely the toes, and are generally conjoined with other leprous symptoms. The nervous disorders confirmed in a few cases of ainhum are by no means characteristic of leprosy, but comprise disturbances that are apt to be set up in the most various diseases of the nervous system, and seem to indicate that in ainhum a *tropho-neurosis* may be present. The lumbar pains observed by Dupouy in his patients seem to have some connection with this cause.

Despetits and Corre regard ainhum as a circumscribed, circular (*i.e.,* linear) *scleroderma*.

The disease predominates in the *male sex*, in *youth* and in the *prime of life*, but it is also observed in women and children. Guyot saw a case in a child of six weeks old ; perhaps this, however, was a case of congenital amputation.

Heredity plays some part in the etiology of ainhum. Da Silva Lima states that he knew a few negro families of whom every member was attacked by the disease. The case observed by Duhring related to a negro whose father had lost two toes from ainhum, and whose mother at the time of his illness was also suffering. Dupouy communicates the case of a negro, whose father and two of whose brothers had likewise had the disease.

DIAGNOSIS.

The diagnosis of ainhum should present no difficulties. Its relations to *lepra mutilans* have already been mentioned above. It is, however, possible to mistake it for Raynaud's *symmetrical* gangrene.

PROGNOSIS.

The prognosis of the disease in regard to life is good.

TREATMENT.

The only treatment consists in the removal of the pendant member by means of the knife, scissors, or by ligature with a string.   At the commencement of the ailment, and before the constriction is very pronounced, an effort may be made to resist the encroachment by deep vertical incisions in the constricting circle.   Da Silva states that a complete cure has been accomplished in some cases by this means.

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VI.—THE COSMOPOLITAN DISEASES IN THE TROPICS.

HAVING in the previous chapters discussed the diseases peculiar to the warm countries, I shall now proceed in the following pages to briefly describe the occurrence and relation of the endemic diseases appertaining to all zones, and which have therefore been appropriately designated *cosmopolitan diseases ;* in this connection the diseases occurring in subtropical countries will incidentally be considered for purposes of comparison.

The different climatic conditions which prevail in warm countries, the various races which are there attacked, and the divergent conditions of life and civilisation found in the tropics, would *a priori* have an influence on the characteristic features of many ordinary ailments. I shall not consider minutely in this chapter the geographical distribution of disease, but refer the reader to Hirsch's classical work ; nor shall I mention the source of information, as the data referred to here are too scattered and multifarious.

I commence with the *infectious diseases*, which always occupy a prominent position in geographical pathology.

TYPHOID.—At a time when every fever occurring in the tropics was regarded as malaria, the opinion prevailed that hot countries were quite immune from this disease. More recent observations, however, have proved that this view is untenable, and that, on the contrary, typhoid rages extensively in the tropics and is more severe in type and more liable to relapses than in Europe. On the other hand, however, remarkably mild typhoid attacks occur, and to these the cases observed by the Italians in Massana (camp fevers) that seldom last longer than a week, and some of the so-called climatic fevers, appertain. Typhoid in the tropics exhibits local and periodical variations in the same manner as in temperate climates. In the dark races, however, the roseola, as may be imagined, easily escapes observation.

EXANTHEMATOUS TYPHOID has hitherto not spread extensively in tropical and subtropical countries. Epidemics of the disease have been observed in Tunis, Algiers, Nubia, Persia, and also in Central and South America. The skin of the dark races renders it difficult to recognise the exanthem, or even conceals it entirely.

RELAPSING FEVER and BILIOUS TYPHOID, which are only modifications of the same disease, are far more largely distributed. British India is one of the most important centres of these diseases, which are observed to be particularly prevalent there in periods of famine.

Chastang identifies a disease occurring in Korea and there called *Im-pyeng* with relapsing fever, although relapses do not seem to be present in it.

The disease sets in between February and July, and particularly affects poor people living under unfavourable hygienic conditions. It is accounted very contagious, so that the patients are often left unattended.

The ailment commences with headache, backache, or vague pains, which are frequently very severe, and which are followed by fever that occasionally rises to 41·5°, exhibiting morning remissions and occasionally delirium.

The illness lasts from seven to ten days. In favourable cases intense perspiration sets in on the sixth or seventh day and after from twenty-four to thirty-six hours defervescence occurs. Great feebleness and cardiac weakness follow, frequently also bronchitis, and from these ailments the patient makes a slow recovery.

CHOLERA although endemic in certain tropical countries is carried into other zones by human intercourse, where it behaves in the same manner as in the tropics, stamping it as a cosmopolitan disease. It is described in every manual and text-book of special pathology and treatment, and for this reason I have not considered it in this book.

MEASLES occurs in all climates. The reason that some few regions, such as, for instance, New Caledonia, have hitherto remained unvisited, or are but rarely the seat of epidemics, is that the disease has either not been carried in at all or has not spread in consequence of the limited intercourse. The course of measles in the tropics is mostly mild. The great ravages made by the disease in a few epidemics amongst uncivilised populations—about one quarter of the population on the Fiji Islands succumbed to measles in 1874—may be attributed less to the severity of the disease than to lack of care and treatment.

SCARLET FEVER, in contradistinction to measles, is generally very scarce in the tropics or quite unknown. It is observed very rarely in British India. It occurs most frequently amongst European children, in Shanghai (in Hong Kong only imported cases are seen), in Java, and on the Congo. Singapore, Bangkok, Tonquin, Annam, Cochin China, Manila, Borneo, Natal, Western Australia, the Tonga and Samoa Islands, Honduras and many other places are free from it. In North America scarlet fever is rarer and milder in the Southern than in the Northern States, and whites are attacked more frequently and more severely than negroes and Indians.

SMALLPOX is extensively disseminated in the tropics. In some countries it is a veritable scourge, as in Central Africa, where wars, expeditions, pilgrimages and commercial caravans contribute to its spread. According to Steudel about a half of all natives fall victims to this scourge.

The black races generally are very susceptible to smallpox, not only in Africa, but everywhere where the disease develops, and the course of disease with them is a severe one. As might be expected smallpox exhibits a different aspect on the negro's skin than on the white man's. First of all papules the size of lentils with œdematous areas and small depressions in their centre develop, and these papules are transformed into pustules without change of colour. In mild cases the pustules heal with circumscribed cicatrices without leaving depressions, and in a month or two they have again acquired the normal pigment of the skin. Even in severe cases irregular depressions only are left permanently, but without change of pigment, near the nose and mouth and on the forehead.

The prophylactic effect of *vaccination* in the tropics, judging by experiences collected in Africa, affords the same protection as with us, but the immunity acquired against smallpox, as well as against repeated inoculation, is supposed to be less lasting; and this is also the case as regards immunity acquired from having had the disease. Repeated attacks and repeated efficacious inoculations in the same individual are not rare.

A. Plehn states that in negroes of the West Coast of Africa the efficacy of vaccination after twelve months can only be reckoned on in a fraction of the cases, and after the expiration of two years only exceptionally.

The course of vaccination is more rapid in torrid than in temperate zones.

It is very difficult to obtain active vaccine, as lymph is injured by its transport to the tropics. In fact if it has to pass through the Red Sea during the hot summer months, its efficacy may be partly, or entirely, lost. Even also in inoculations from calf to calf, a lessening of the virulence of the lymph is apparent after repeated transmissions; this is also the case in continuous inoculations from arm to arm. In Saigon and British India buffalo lymph has proved of far greater efficacy and durability than calf lymph, whereas in the Dutch Indies the experience has not been equally good. In British India the addition of vaseline to the lymph has proved of value in preserving it, and it possesses the additional advantage of not being affected by the heat.

CHICKEN POX occurs in the tropics, although but rarely mentioned in medical reports.

ERYSIPELAS is relatively rare in the tropics. I have likewise observed it but rarely in Japan. In the coloured races the exanthem does not cause any change of colour of the skin.

DIPHTHERIA is not a common disease in the tropics and mostly exhibits a mild character. In some places, such as Singapore and Bangkok, it does not occur at all. There does not appear to be any racial immunity, but Europeans are more often attacked than natives.

SEPTIC and PYÆMIC DISEASES are rarely observed in the tropics; this is perhaps attributable to the strong sunlight, which has a bactericidal effect.

PUERPERAL FEVER occurs with considerable frequency, especially after parturitions in which native " wise " women have rendered assistance. In Java, according to Strauss, puerperal fever is supposed to be even more frequent than is the case in Europe.

TETANUS is extensively distributed in the tropics. The natives have a remarkable susceptibility to it; but this is at least partly explained by the circumstance that they are particularly liable to injuries on account of their scanty clothing, and their habitual indolence causes them to neglect small wounds. Some districts are particularly liable to this disease. As an instance, until within a few years ago in the Island of St. Kilda, belonging to the Western Hebrides, the ailment was so frequent that from one half to two-thirds and more of all newly-born infants succumbed to it, and in consequence it was called " the scourge of St. Kilda."

PNEUMONIA is very unevenly distributed in the tropics. Thus it is very frequent in Cameroon and on the Congo, particularly in negroes, whereas in the Dutch Indies severe inflammation of the lungs is hardly ever observed in natives. According to my experience in Japan, also, croupous pneumonia is a rare disease.

WHOOPING COUGH is likewise frequent in some tropical countries; in others, on the contrary, it is rare, or utterly unknown. In 1895, according to A. Plehn, the first epidemic of this disease was observed on the West Coast of Africa. It sometimes appears in a very severe form. In the epidemic of 1883 occurring on the Fiji Islands, 3,000 natives are said to have succumbed to it.

INFLUENZA in its wanderings visits the tropics in the same manner as it does the higher latitudes.

EPIDEMIC PAROTITIS is exhibited within the tropics with unequal frequency. Thus it is found very frequently on the West Coast of Africa,

but is not known in Manila and Singapore. Its course, as a rule, is very mild.

The distribution of ACUTE ARTICULAR RHEUMATISM is similar to that of epidemic parotitis. It does not occur in Bangkok, Manila and Stanley Pool, and is rarely observed in Central America, on the Antilles, Java and Penang. In British India it is seldom met with in natives or on the plains, while in the hill stations it is supposed to be as prevalent as it is in Europe. It occurs frequently in Singapore, Cochin China and China, but it is very rare in Japan. In Cameroon it is fairly frequent in Europeans as well as in natives.

CHRONIC RHEUMATISM and MUSCULAR RHEUMATISM are, it may be mentioned, ubiquitous diseases in the strictest sense of the word. There is a great tendency to chills in the tropics, in natives as well as in Europeans.

TUBERCULOSIS shows a different condition in different tropical countries. In any case the opinion formerly expressed, that this disease is more frequent in torrid than in temperate zones, has no validity. There are districts in which it is of common occurrence, and others where it is either entirely absent or very rare. It is largely distributed in British India, more especially amongst the natives. It is also frequent amongst the natives of Manila and the New Hebrides. On the other hand, it is seldom met with on the west and south coasts of tropical Africa; in Cameroon, indeed, it is, according to A. Plehn, quite unknown. In this respect, however, the reports of separate observers do not coincide. In contradiction to A. Plehn, Zahl states that tuberculosis is frequently met with in Cameroon. The distribution of this disease in the tropics is more governed by the density of the population, conditions of housing and feeding, and the absence or presence of industries, than by climatic or racial peculiarities. It is also observed in the tropics that the disease is of rarer occurrence in a dry climate than in a damp one, and that high altitudes have a favourable influence.

The assertion that the course of tuberculosis in the tropics is by far more rapid than with us, is also incorrect. For instance, it is reported from Manila that the course of the disease is slower there than in Europe.

That which has been said above also holds good for pulmonary tuberculosis. Little has been mentioned in medical reports about articular- and osteo-tuberculosis.

In a few reports the absence of LUPUS is remarked upon, as in Bangkok, Singapore, Java and Madura, although tuberculosis is of frequent occurrence in these places. In Japan also, where not only tuberculosis, but also scrofula, bony caries, articular inflammations, &c., are very frequent, lupus does not seem to occur, at least I have never met with such a case. In Manila and on the Fiji Islands where tuberculosis is frequent, lupus is not uncommon.

SYPHILIS is distributed nearly all over the tropics. It is only absent in the districts that have not been opened to commerce. It is a sad fact, and one that cannot be denied, that the advent of foreigners into remote countries has introduced not only the blessings of civilisation, but the curse of syphilis. The negro races of the interior of Africa that are still untouched by commerce are free from the disease, and it is also supposed to be very rare in Cameroon. Moreover, commerce and syphilis have not yet reached the natives of New Guinea.

The course of this disease varies in the tropics. Sometimes it does not deviate from syphilis as observed in Europe; sometimes, as in tropical

America, it is more severe; sometimes, as in various parts of tropical Africa, it is remarkably mild. This shows that climate alone exercises no influence on its course. Perhaps, however, besides the kind of, or lack of, treatment, race may have some influence. The black race seems to possess a certain immunity; the course of syphilis in them is in general a mild one. It is also decidedly remarkable that in those parts of Africa where the scourge is being imported, as, for instance, in the Congo State, it does not cause great epidemic ravages as in other newly discovered countries. In Madagascar, on the other hand, the disease appears in a form reminiscent of syphilis of the fifteenth century, its transmission being even effected by non-sexual intercourse. At all events, the disease there known as *tety* is indicated as of this character.

Reports from a few countries, such as Sumatra and the Marshall Islands, state that the disease rapidly assumes the tertiary stage. On the Marshall Islands the tertiary symptoms are sometimes seen in natives (not in Europeans) only a few months after infection, whereas secondary symptoms are not observed.

I have made similar observations in Japan where syphilis is very widespread, but is not, generally speaking, more severe than in Europe. I very seldom observed maculo-papular syphilides in Japan, but this is perhaps explained by the darker pigmentation of the skin; in place of this, however, there is often pustular-impetiginous exanthems which mark the transition into the tertiary stage. Moreover, in the secondary stage pains in the bones and joints occur, and tertiary symptoms (gummata, ulcers, and affections of the bones) are apt to set in very early.

The assertion was formerly made that syphilis, when transmitted from one race to another, was particularly severe. No support is given to this view in the most recent literature, and observations made by myself and others in Japan also failed to confirm the statement.

SOFT CHANCRE and GONORRHŒA with their sequelæ are found everywhere in the tropics. As may be gathered from the publications on the subject, they have for ages been classed with the ubiquitous diseases. In regard to venereal buboes it may be remarked that they sometimes set in with, and their course is accompanied by, high fever. In Chili scrotal abscess is often observed as a consequence of ordinary gonorrhœa, attributable to the fact that the Chilians, even when affected with the ailment, are accustomed to be all day on horse-back.

As to DISEASES COMMUNICABLE FROM ANIMALS TO MAN, HYDROPHOBIA is by no means uncommon, and West Africa, India, Malacca, Annam, the Dutch Indies and tropical America, belong to its geographical regions of distribution.

As yet there are no accounts of the occurrence of glanders and anthrax in the tropics.

INSOLATION and HEAT APOPLEXY are in general far less common within the torrid zone than one would *a priori* be led to expect. In some of the hottest countries they do not occur at all, or only very rarely come under observation. The reason for this is in all probability due to the precaution with which Europeans in the tropics usually protect themselves from the direct influence of the sun's rays, and generally avoid bodily exertion; if, however, they have to be exposed to the sun, as in the case of soldiers, they should be suitably clothed and above all should not be burdened with baggage. Sambon, in consequence of the geographical distribution exhibited by insolation, which does not always coincide with a high temperature, has formed the opinion that insolation, or at least a certain form of the disease, is not to be regarded as a direct consequence

of heat but as an infectious disease which he designates *siriasis*. The form he alludes to is characterised by hyperpyrexia, profound coma, contracted pupils and severe pulmonary congestion ; these symptoms are usually preceded by prodromal symptoms and followed not rarely by relapses. Sambon has, however, hitherto not gained many supporters for his hypothesis.

In regard to CONSTITUTIONAL DISEASES, *rickets* are very rare in the tropics, and are even unknown in many countries. In Japan I have never observed the disease. Coinciding with the present views as to the etiology of the disease, the reason for this immunity is no doubt attributable to the circumstance that tropical children always get plenty of fresh air and sunlight, though the fact that infants are usually suckled, and suckled for a very long period, is of importance in this connection. At all events the scarcity of rickets in the tropics proves that malaria, as has been asserted, plays no part in its etiology.

SCURVY is not widely distributed in the tropics. In some countries it is frequent, as in Yemen (Arabia), in Java where the disease has been particularly observed after bad rice harvests, in British India where prisoners in gaols are particularly affected by it, in Cochin China, the northern districts of China, on the west coast of Africa, in the Eastern Soudan, and in Western Australia. In other regions, as in Singapore and Manila, on the other hand, it is unknown. In Japan, one case only came under my notice. Scurvy is quite independent of climate, but is intimately connected with food. Formerly it was an equally frequent guest in Polar and Equatorial seas on board ships making long voyages.

DIABETES is reported as a frequent occurrence in various tropical countries. In Ceylon and British India it is more frequent amongst Europeans than in Europe, and it is still more frequent in the case of natives than it is in Europeans. It seemingly, on the other hand, does not exist in tropical Africa, and this is probably also the case in Central and South America. I have observed a limited number of cases in Japan.

GOUT, as a rule, is very rare, or entirely absent, in the tropics. In India it is only observed in Europeans and Mohammedans, not in Hindoos. In Japan I never observed a case. That the rarity of gout in warm countries is not alone due to the moderate manner in which natives live, whose staple diet consists of vegetables and who rarely partake of alcohol, is proved by the extreme rarity or absence of the disease in warm countries such as Brazil, where the inhabitants are in the habit of living luxuriously.

GOITRE, with and without *cretinism*, is endemic in many tropical districts, mountainous as well as flat. No race or nationality seems to enjoy immunity from these affections. Only of the Dhanghours, the natives of Chota, Nagpore, Lower Bengal, who are supposed also to possess a considerable power of resistance to malaria, is it reported that they seldom if ever are attacked when they go as labourers to the most notoriously goitre districts.

CANCER is rare in the tropics. It is only in a few countries, such as the Antilles (Martinique, Barbados) and in India, that it is met with, though even in these it is far more rare than in Europe. In China, on the other hand, it is no rarity, and the same may be said of Japan, where I personally operated on a large number of cases, the majority of which occurred in the female mammary gland.

OF DISEASES OF THE RESPIRATORY ORGANS, *bronchitis* is of the most frequent occurrence, the disease being particularly frequent in negroes. Pneumonia and tuberculosis have been considered above.

We know little of the DISEASES OF THE ORGANS OF CIRCULATION. In Europeans, *functional heart ailments* come under observation, and heat seems to play an important part in their etiology. In choosing persons for service in the tropics it is therefore necessary to make a careful examination of the heart and vessels.

DEFECTS OF THE CARDIAC VALVES occur frequently in some countries in which acute articular rheumatism is rare, as in British India. Other causes must therefore be taken into consideration. It is reported from Buenos Ayres that heart disease, especially aortic disease and aortic aneurism, is very frequent in the negro population. Chronic *endarteritis* and *aortic aneurism* are frequently observed in Europeans as well as in natives, in India, China, Brazil and Chili. Aneurism of the aorta is likewise remarkably frequent in Japan, a circumstance which, according to my observations, is largely due to syphilis. The reports from various countries, however, do not mention whether this is the case elsewhere.

As to the DISEASES OF THE DIGESTIVE ORGANS, *gastric* and *intestinal catarrh* are more frequent in the tropics than in Europe, and affect both Europeans and natives. With regard to the symptomatology and the pathological changes met with in these complaints, they exhibit no material differences from those of the temperate zone, with the exception that they more frequently assume a chronic character, causing emaciation, anæmia and frequently death. Their frequency is explained by the sensitiveness of the intestinal canal peculiar to the tropics, and attributable to the altered conditions of the circulation and the atony of the intestinal muscles, rendering the mucous membrane of the intestine more easily affected by the effects of infectious lesions than they would be under normal conditions.

Errors in diet, contributed to by the rapid decomposition of articles of food and by the tendency to chills, furnish incidental causes.

It was previously mentioned that Bertrand and Fontan identify chronic diarrhœa of the tropics with chronic dysentery.

A disease that appears on the west coast of South America (between Valdivia and Arica) during the hot summer months, and which is there known as *lepidia*, appears to correspond with our *cholera nostras*.

HÆMORRHOIDS are an ailment to which Europeans living in the tropics are liable, and are apt to be set up as a concomitant of tropical liver. Negroes are very rarely affected.

INTESTINAL PARASITES are remarkably frequent in the tropics. Besides the parasites peculiar to warm countries that have already been discussed, *ascaris lumbricoides, oxyuris, vermicularis, trichocephalus dispar, tænia solium, tænia mediocanelleta, bothriocephalus latus,* which are endemic in Europe, are met with everywhere in the tropics, especially amongst natives. Climate and race have less influence on the spread of these parasites than the kind of food and the sanitary conditions of the various nations. The intestinal canal being, as already mentioned, more sensitive in the tropics than in higher latitudes, reacts more severely to the parasites, causing more serious disorders than one usually observes in Europe. It is therefore advisable in the tropics to examine the stools of patients suffering from intestinal disorders for the ova of parasites.

I may at this point consider other parasites. *Trichinosis* is exceptionally rare in the tropics. Formerly a few cases were reported from Calcutta. In Japan, the disease has come under observation a few times in foreigners who had eaten the meat of swine imported from China. The disease therefore is probably indigenous in China, where pigs play an important part in the diet of the people, although medical reports

thereon are not forthcoming; it is even not improbable that trichinosis originated in China, for the discovery of the disease in man in Europe took place towards the end of the third decade of last century, almost simultaneously with the introduction of small Chinese pigs into Europe.

The occurrence of the *echinococcus* is very limited in warm countries, as it has hitherto only been met with in India, Algiers, Egypt and Victoria (Australia).

There is but little to be said respecting the DISEASES OF THE URINARY APPARATUS. In some tropical countries *kidney diseases* are very frequent. Chills, caused by scanty clothing, draughty dwellings, and malaria, are etiological factors, as already mentioned. The frequency of *urinary calculi* in certain tropical countries has also been considered.

In regard to the DISEASES OF THE NERVOUS SYSTEM we have already seen that the influence of the tropical climate on the nervous system of *Europeans* is principally manifested in *sleeplessness* and *nervous irritability*, which, particularly if in conjunction with the effects of malaria, may develop to considerable neurasthenia. Such patients exhibit boundless excitement, to which they were formerly not subject, so that they are carried away to perform acts of violence and other unpremeditated deeds; such explosions are as a rule followed by extreme exhaustion. If the derangement proceeds further, the symptoms of irritation generally give way to symptoms of paralysis of certain nervous centres. The most prominent symptoms are extreme apathy; an aversion to all mental work, and an irresistible desire to sleep after every meal. A few patients complain of giddiness, pressure in the head, headache, oppression in the chest, indefinite sensations of anxiety, more or less precordial agony, nervous palpitation of the heart; sometimes also there is nervous dyspepsia. The moods vary considerably, gliding into the extremes of joy and sorrow on the slightest cause; on the other hand, the patient may bear the strokes of misfortune with a sort of resigned stupor; later on, hallucinations may set in.

In the initial stage of this disease F. Plehn recommends that the patient take plenty of exercise in the evening, that he drinks a bottle of stout, that he has a cool douche, or a bath just before retiring to rest, but above all that the bed be so placed that the patient is fully exposed to the influence of the breeze. Should these measures fail to afford relief, a change of air (a sea voyage, a sojourn on the hills, or return home) is urgently necessary. The use of soporifics, especially morphia, is to be stringently prohibited. Neurasthenic sleeplessness has been the principal cause of the spread of the morphia habit in some of the colonies.

The unfavourable effects of tropical climates on the nervous system are still further increased if contributed to by other predisposing causes, such as heredity, excesses, exhausting diseases, insolation, or other circumstances originating nervous disorders. Rudimentary or fully developed *mental derangements* may then ensue. Mental diseases, therefore, are, according to Rasch, more frequent in Europeans in the tropics than in temperate climates. Persons possessing any predisposition whatever to nervous diseases are unsuitable for service in the tropics.

The particular psychological disorder designated *tropical frenzy* by laymen, does not exist, though to this is ascribed the deficiency of moral sensibility occurring in the insanity which is frequent in the warmer climates. On this subject Mense, with justice, expresses himself as follows: "The alleged disorder, has been expressly fabricated by laymen according to whether the affected persons are governed by pleasure or hatred. There are, relatively, a great many eccentric characters amongst

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Europeans living in the far distant colonies, for the quiet ordinary man prefers to remain in his comfortable native land. The opportunity is afforded in isolated and distant lands for the weak characters to lose their moral equilibrium; in Europe they are under the stern eye of the law, and of society, and custom compels limitations to one's conduct. The same type of persons who suffer from the so-called tropical frenzy in the colonies are inclined to excesses everywhere, even at the North Pole, as soon as the strait-jacket of civilisation is loosened."

Perhaps " *Soudanite*," a disease stated to be due to the effect of heat in conjunction with malaria, appertains to the same category of disease as tropical frenzy. The condition is thus designated in consequence of the mad acts of two French officers in the French Soudan, who fired on their native flag and killed two of their comrades and part of their escort.

" Soudanite " is supposed to commence with melancholia, slight fever and anæmia. Moral and mental derangements, assuming different forms in different individuals, follow. Some scream and fire off their pistols repeatedly at some object that appears to disturb them. Others go about dressed in heavy black clothing in spite of the heat. All patients, however, become confused and incapable of reasoning and exhibit wild moods. Even men who previously had the most placid disposition develop violent quarrelsomeness under the influence of this peculiar ailment, which is sometimes supposed to set in epidemically and attack entire companies. It has repeatedly occurred that entire expeditions have halted in the desert of Sahara and have wasted precious hours in senseless disputes on trivial subjects.

A great many children of European parents die in the tropics from *eclampsia*, malaria being its most frequent cause. The disease is also not uncommon in the children of natives.

We know but little of the nervous diseases of the *natives* of tropical countries, but we are aware that different races, especially as regards mental diseases, exhibit considerable differences, attributable, no doubt, to racial peculiarities, or the different surroundings in which the various nations have been born and reared.

In African *negroes* living in a primitive condition, mental diseases are remarkably rare; but the disposition to insanity is enhanced through civilisation, and the consequent intensified mental activity which life in foreign parts entails. Since the emancipation of slaves mental disorders have greatly increased amongst the coloured folk of North America, mania being the predominant feature. Suicide is very uncommon amongst them. Hysteria is not uncommon in negroes, even in their primitive state. Mental disorders are rare amongst other blacks (Australians, Melanesians, and Negritos).

On the other hand, dementia is very prevalent amongst the Malays, who possess abnormally excitable nerve-nutrition, so that trifling causes are sufficient to disturb their mental equilibrium. In correspondence with their insipid, monotonous mental life, hallucinations in the insane are only rudimentarily developed, while "motoric " attacks are a prominent feature. There is seldom a tendency to suicide and refusal of food. On the other hand, the dementia frequently exhibits periodicity and indications of degenerative insanity, which, however, according to van Brero, whose statements I quote, are rather to be attributed to imperfect mental development in the ethical and intellectual direction than to a racial degeneration.

Amentia is the most frequent form. Monomania and dementia paralytica are rare, and van Brero has never observed melancholia.

Epilepsy, which is very frequent in other warm countries, in India,

Further India, and Ceylon, is a rare disease amongst Malays, and the same holds good of tabes.

van Brero also remarks upon the rarity of decubitus and othematoma in insane Malays, and ascribes this to the high temperature which favourably influences the condition of nutrition of the skin.

As to the *Mongolians*, mental disorders are supposed to be uncommon amongst the *Chinese*. In the *Japanese*, on the other hand, all forms of dementia occur, mania being more frequent than melancholia. These people also frequently suffer from hysteria and epilepsy, whereas, according to my experience, progressive paralysis, as also tabes, are rarely observed. This is the more remarkable because, as mentioned above, syphilis is widely disseminated in Japan. Correspondingly, progressive paralysis and tabes are rarely or never met with in half or quite uncivilised nations, notwithstanding the frequency of syphilis, a circumstance from which one may conclude that syphilis is not the only cause of these two diseases, but that other etiological factors, to be sought in our modern civilised life, combine with it in originating these disorders.

SKIN DISEASES, and more particularly parasitical skin diseases, are remarkably frequent in the tropics, in natives as well as in Europeans, the condition of irritation of the skin induced by the heat, preparing the soil for the parasites. This holds good equally for *scabies*, for *pityriasis versicolor*, for *erythrasma* and for *ringworm*.

Ringworm is a variety of our herpes tonsurans, from which, however, it is differentiated by its rapid growth, and by the circumstance that it mostly attacks the non-hairy parts of the body, and that, when it attacks the hairy parts, it does not cause the hair to fall out. Probably, as in herpes tonsurans, the disease is originated by various fungi. The inguinal and gluteal region and the axillary cavities are attacked most frequently, the head and limbs most rarely. In hot damp weather it is an exceedingly troublesome disorder in consequence of the unbearable itching that it causes. During the cooler season it may disappear entirely for a considerable period, even without having been treated, though secondary infection, which may take place through the small wounds made by scratching severe skin diseases, such as furuncles and abscesses, may be set up. Goa powder (chrysarobin) is the sovereign drug for ringworm.

In India, this ailment is usually called *dhobie* itch (washerman's itch). This designation, however, is not used for ringworm alone, but for every itching affection of the skin, such as pityriasis versicolor and erythrasma, which have a ringworm-like appearance. This skin disease is called dhobie's itch, because it, by predilection, attacks the dhobies (washermen), who are infected by the washing of soiled linen of persons suffering by the disease, and then spread it by means of the linen passing through their hands.

In my opinion *pemphigus contagiosus*, described by Manson as a tropical disease, is identical with our pemphigus acutus. This ailment principally attacks children, is very frequent in South China, the Straits Settlements, Madras, and probably occurs all over the tropics; I have also observed it in Japan.

In the older publications the great frequency of *psoriasis* in the tropics was reported upon, but it was seemingly confounded with the above-mentioned epiphytic diseases. Recently reports have been published according to which psoriasis does not appear to occur in a few tropical districts, such as Bangkok. I also failed to observe the ailment in Japan.

Furuncles are remarkably frequent in the tropics, especially during the hot season, and they even sometimes occur epidemically. They may

appear on all parts of the body with the exception of the palms of the hands and the soles of the feet, and they exhibit a far more acute course than the furuncles of temperate climes. In Egypt they are called *boutons du Nil*, and in the East Indies *mango* boils, although they have as little connection with the Nile water as with the mango. F. Plehn demonstrated the staphylococcus pyogenes aureus in furuncles.

In the black and yellow races *keloids* are frequently encountered; they come into existence after trifling wounds and ulcers (ear-piercings, inoculatory cicatrices, subcutaneous injections, sutures, pustules and boils), and are certainly largely attributable to defective and unclean treatment of wounds. On the ears the keloids sometimes cause the formation of disfiguring tumours as large as billiard balls, or even larger.

Vitiligo, often extensively distributed over the body, is also not uncommon in coloured people. In a few countries, such as India, actual Albinos are met with remarkably frequently.

DISEASES OF THE EYE are universally frequent in the tropics. The diseases of the conjunctiva and cornea predominate. *Blenorrhœa* and *trachoma* are remarkably frequent. The former in some countries, as in Japan, is next to small-pox the principal cause of the number of blind persons. To trachoma the different races appear to have a diverse predisposition. According to Yarr, the native races of Canada, including the Esquimaux, possess entire immunity; the negroes and Singalese possess relative immunity; on the other hand, the white races are susceptible to it, and especially the Jews, Poles, Italians and Irish. The Chinese and Japanese, however, are supposed to possess the greatest predisposition to the disease.

Xerosis conjunctivæ is, moreover, a frequent disease in tropical and subtropical countries; as a rule it is connected with *hemeralopia*, and weakness of sight in diminished light; its cause is decrease of the general condition of nutrition in conjunction with glare. A severer form, complicated with keratomalacia, is frequently observed in the native quarters of tropical towns such as Bombay, Calcutta and Hong Kong.

Hemeralopia not rarely occurs as an independent disease in consequence of the influence of the vivid sunlight, more especially on the sea and in arid districts without vegetation. In a few nations, as for instance, the Melanesians, the disease appears to be very frequent. Ouwehand found it in the natives of Toba (Sumatra), who often suffer from it and call the disease *rondar manok—i.e.*, hen-blind; it is usually associated with slight albuminuria.

A. and F. Plehn occasionally observed *nyctalopia* in Cameroon as well as in German East Africa as a consequence of the dazzling light; the weakness of sight amounting to almost entire day blindness, lasted for weeks and months, but which was as a rule curable by means of suitable treatment, namely protection from light. In addition to slight redness of the conjunctiva, a slight inflammation of the retina could only exceptionally be demonstrated; the result of ophthalmoscopic inspection was mostly negative.

I am myself aware how defective and incomplete the above statements are. They, however, represent in brief what I have personally observed on the subject and what I have gathered in the literature known and accessible to me.

Perhaps these lines will give the impetus for further publications which will contribute to the demands on our knowledge as to the occurrence and condition of the cosmopolitan diseases in the tropics.

ADDENDUM TO CHAPTER ON YELLOW FEVER.

BY JAMES CANTLIE, M.B., F.R.C.S.

OUR knowledge of yellow fever has been advanced considerably since Scheube's work appeared, as the result of the investigations of the U.S. Army Commission on the Island of Cuba during the years 1900 and 1901. The chief points brought out by the experiments conducted by the members of the Commission are as follows :—

I.—*No Bacterium of any kind could be detected in a cultivated form, in the blood of persons suffering from Yellow Fever.*—In view of the many organisms that have been from time to time announced as causative of yellow fever, this is a most important statement. Previously to the investigations of the Commission all the bacteria alleged to have been found in the blood of yellow fever patients had been practically refuted, with the exception of the Bacillus icteroides of Sanarelli. Careful investigations concerning the presence of this bacillus, or in fact of any organism, bacterial or protozoan, gave negative results.

II.—*Infection by Fomites. Attempts at infection by Fomites gave negative results.*—In a specially prepared house, with every other means of conveyance of yellow fever guarded against, healthy (non-immune) persons were made to sleep in beds in which blankets, mattresses, sleeping apparel, pillow cases, &c., had been used by, or saturated with the excreta, vomit, &c. of, yellow fever patients. Although a lengthy exposure was kept up, amounting to several weeks, none of the persons thus exposed contracted the disease. So thoroughly and scientifically was this experiment carried out that the negative influence of fomites in regard to the spread of yellow fever must be regarded as settled.

III.—*Infection by Mosquitoes. Positive results were obtained as to the spread of Yellow Fever by infected Mosquitoes.*—The experiment was carried out in a newly erected building, where twelve healthy persons were shut up and exposed to the bites of mosquitoes, belonging to the species Stegomyia fasciata, that had already fed on yellow fever patients. Ten of the twelve persons thus experimented on contracted yellow fever. Control experiments were carried on contemporaneously by submitting non-immune persons in the same building, but guarded from mosquito bites by a mosquito-proof screen; no person thus protected contracted the disease.

IV.—*Period of Incubation in the Mosquito.*—A period of twelve or more days must intervene between the time the mosquito imbibes the yellow fever poison and the time it can infect by its bite non-immune persons. Mosquitoes, however, that had been kept for from thirty-nine to fifty-

seven days after contamination, proved capable of conveying the disease. Further, infected Stegomyia fasciata may survive for a period of seventy-one days after having absorbed the yellow fever poison.

V.—*The Blood of Yellow Fever Patients, when inoculated into healthy (non-immune) persons, causes Yellow Fever.*—This is true, whether the fresh blood from a vein of a person suffering from yellow fever be injected into a healthy (non-immune) person, or whether the blood be partially defibrinated.

VI.—*Bacteria-Free Serum Filtrate, injected into a healthy (non-immune) person, causes Yellow Fever.*—When blood drawn from a case of yellow fever and diluted with sterilised water, is passed slowly through a Berkefeld laboratory filter (through the pores of which no known bacterium can pass), the diluted serum thus obtained caused yellow fever when injected into the vein of a healthy (non-immune) person. This experiment serves to confirm, as far as our present laboratory methods of investigation can do so, that yellow fever is not due to the presence of a bacterium.

VII.—*The Specific Agent which produces Yellow Fever is destroyed by exposure to a temperature of 55° C. for ten minutes.*—It may be that the specific agent is not wholly destroyed, but only so attenuated that even 1·5 ccm. of the blood which had been so heated failed to produce the disease when injected into a non-immune person.

These several experiments prove :—

(*a*) That the virus of yellow fever is contained in the blood.

(*b*) That the specific agent in producing the disease is destroyed or attenuated by exposure to a temperature of 55° C. for ten minutes.

(*c*) That yellow fever is not caused by a bacterium in the blood.

(*d*) That the disease is not spread by fomites, but by a mosquito.

Prevention of Yellow Fever.—The logical outcome of the above statements and conclusions is that "the spread of yellow fever can be most efficiently controlled by the measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects." The practical application of the principle adduced in this axiom, also proved wholly satisfactory. Every yellow fever patient in Havana was not only quarantined, but the room in which the patient lay was protected with wire-screens, so that mosquitoes could not reach the patient, or having reached him could not escape.

The mosquitoes, also, in other rooms of the house in which patients lay, and in the houses immediately adjoining, were destroyed by various methods, with the result that Havana was, for the first time for some forty years, freed of the disease.

It would appear, therefore, that the quarantine regulations in force against yellow fever require modification, if not complete revolutionising.

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ADDENDUM TO CHAPTER ON MALARIA,

FROM JULY, 1900, TO OCTOBER, 1902.

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SINCE Dr. Scheube wrote this article much work has been done in connection with malaria and mosquitoes. Numerous observers have proved conclusively that malaria is carried by mosquitoes belonging to the genus *Anopheles,* and all experimental attempts with other mosqitoes have failed.

It has been further shown that the phases, in the mosquito, of the human malaria parasites are in all main points identical with those completely described by Ross for the proteosoma and previously in part described for the human parasites by him.

It has been proved that persons living in an intensely malarial place, but completely protected from mosquito bites, do not contract malaria,[1] showing that the mosquito is, if not the only infecting agent, at any rate the important one.

Malaria has been contracted by men in non-malarial countries[2] when bitten by mosquitoes infected with malaria elsewhere, imported into the non-malarial country. In all cases the type of fever contracted by persons bitten by mosquitoes purposely infected has been the same, benign tertian, as that of the person from whom the mosquitoes derived their infection.

Although all the mosquitoes so far proved to carry malaria belong to the genus *Anopheles,* some species belonging to this genus are poor carriers and the malaria parasite rarely develops in them. Such mosquitoes, as for instance, *Anopheles Rossii,* even if numerous, play no important part in the propagation of the disease.[3] *Anopheles maculipennis,* called by Prof. Scheube *A. claviger,* is probably the important carrier only in Europe, the Mediterranean shores and islands and part of North America. In tropical Africa, *Anopheles funestus and costalis* are the chief agents, and in the West Indies and tropical America *Anopheles argyrotarsus.* In India and Asia generally there are several good carriers known.

In all, the number of known species of anopheles is over fifty, but many of them have not as yet been experimented with.

As regards the life history of the mosquito, the most important practical advance is the recognition of the part played by rivers, streams, springs, and large collections of fresh water, when the margins are overgrown with grasses and sedges, as breeding grounds of anopheles.[4]

The evidence that man is the only intermediate host of the malaria parasites has considerably increased, and the recognition that immunity is not racial or constitutional, but acquired by previous attacks, has removed some of the difficulties in accounting for the distribution of malaria.

Many workers in the tropics who had to deal with children were quite familar with the fact that negro children frequently have malaria, whilst adults were exempt, or nearly so. *Post-mortem* examinations in British Guiana had shown that over 80 per cent. of the children of all nationalities and the same proportion of negro children, showed evidence of previous malaria in the shape of melanin deposits in the spleen between 2 and 5 years of age, and also that the fatal convulsions of children were mainly, in that country, due to malaria.[5] Koch[6] showed that even children apparently in good health, frequently harbour malaria parasites. Other observers have confirmed and amplified these facts. It is now known that in countries where malaria is early acquired by new comers, young children of the native races suffer severely from malaria, whilst adults do not. In other countries where susceptible new comers live for years without being infected, the native adults show no such immunity. In brief, the more frequent the opportunities of infection the earlier is the age incidence in the native population. The immunity acquired is not a permanent one, but is probably maintained by repeated abortive infection. Residence in a non-malarial country results in loss of immunity, even amongst the negroes, and probably a prolonged season, such as the winter in the south of Europe when no infections take place, accounts to a large extent for the absence of immunity in adults in Italy.

A more general study of the relationship of enlargement of the spleen to malaria has led to important results. It had been shown previously that the ages at which splenic enlargement is most common did not correspond with ages at which malarial pigmentation of that organ was most common in British Guiana,[7] and that the much enlarged spleens are usually free from melanin. Working in India, Stephens and Christophers have shown that at ages where malarial parasites are commonly found splenic enlargement is not so common as at later ages, and parasites were very rarely found in a large series of patients with enlarged spleens. These conclusions do not hold good for negroes, as enlarged spleens are only common amongst them at ages little greater than those at which parasites are common.

In all other races, Europeans, Chinese, East Indians, South American Indians, &c., the spleens enlarge in malaria, and in a fair proportion of cases residence in a malarial country leads in these races to a chronic progressive splenic enlargement, apparently quite independent of subsequent malarial attacks and persisting and increasing after immunity to the parasite is acquired. Pyrexia, not accompanied by malaria parasites in the blood, is common in such cases and it does not yield to quinine. The "spleen test," as a test of the prevalence of malaria in a country or district is only of value when age and race are also considered.[8]

Much work has been done on the relative proportions of the various forms of leucocytes during malaria, and it has been shown that a marked relative increase in the large mononuclear leucocytes takes place and persists for a considerable period after the parasites have ceased to be found. This leucocytic variation is not affected by quinine, and though sometimes found in other diseases, is a valuable indication of recent malaria. In practice it is of great use, as it enables us to exclude malaria in persons who have been taking quinine for supposed malaria, as in such cases the absence of parasites from the blood is no evidence against

supposition that the case was one of malaria, whilst the absence of this leucocytic variation is conclusive.

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Fig 24.

Fig 23.

Fig 25.

Fig 24.

Fig 26.

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Map I.

THE GEOGRAPHICAL DISTRIBUTION
OF MALARIA
AND OF BLACK WATER FEVER

Malaria ▦ Black Water Fever

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70°

60°

40°

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0°

20°

40°

Map II.

THE
GEOGRAPHICAL DISTRIBUTION
OF BERIBERI

2

70°

60°

40°

20°

0°

20°

40°

20

Map III

THE
GEOGRAPHICAL DISTRIBUTION
OF
LEPROSY

20

70°

60°

40°

20°

0°

0°

20

ARCTIC OCEAN

ARCTIC OCEAN

EUROPE

ASIA

AFRICA

NORTH AMERICA

ATLANT.

China

Japan

India

Further India

Luzon

PACIFIC OCEAN

OCEAN

Ceylon

Seychelles

Mombasa
Zanzibar

Archip.

South Sea Islands

SOUTH AMERICA

Brazil

INDIAN

Mauritius
Reunion

AUSTRALIA

Queensland

New Caledonia

OCEAN

ATLANTIC

THE
GEOGRAPHICAL DISTRIBUTION
OF FILARIASIS

Se

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70

60

40

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G.

20

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Map V

THE GEOGRAPHICAL DISTRIBUTION
OF
ANKYLOSTOMIASIS

CHLOROSENE.

THE MOST CONVENIENT CHLORINE DISINFECTANT.

20 TIMES STRONGER THAN PURE CARBOLIC ACID.

A Reliable Germicide for the Bacteria of Cholera, Bubonic Plague, Yellow Fever, Small Pox, &c., &c.

CONTAINS 4% AVAILABLE CHLORINE.

Does not Coagulate Albumen.

The Best Disinfectant for use in Cities, Camps, and Hospitals.

THE UNITED ALKALI Co., Ltd.,
LIVERPOOL.